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OBSERVATIONS ON EXPERIMENTALLY INDUCED CHOKED DISC.

By Harvey Cushing, M. D., and James Bordley, Jr., M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

As is well known, there have been two conflicting views in regard to the etiology of the characteristic changes in the eye-grounds which accompany cerebral tumors. One of these views accredits the condition to purely mechanical causes of one sort or another; the other, to toxic or inflammatory ones.

Hence the terminology on the one hand indicates a stasis phenomenon—"*Stauungspapille*," "choked disc" or "papill-œdema"; on the other, an inflammatory process which produces what von Leber called a "neuritis" or "papillitis," according as reference is made to the entire nerve or only its intraocular portion. So loosely are these terms used that a number of recent writers speak of the early stage of retinal congestion as an "optic neuritis" which is followed by a "choked disc" when the resultant swelling of the papilla reaches a measurable degree—placed, indeed, by some as high as three or four diopters. If these distinctions are to be drawn it would seem preferable to reserve, as was originally done by Gowers, the term optic neuritis or papillitis, indicating inflammation, for the later stage when round-celled invasion and neuroglial proliferation have occurred as the sequel of a long-standing œdema, and to speak of the primary congestion from stasis as a choking of the disc.

In order to avoid confusions of this sort, it has seemed best to us, whatever designation is to be employed, to indicate the entire process by one term which embraces all grades of the retinal lesion, from the earliest congestion (hyperæmic stage) to the final destruction of the optic fibers (atrophic stage).

For many reasons we have chosen to adhere to Sir Clifford Albutt's well-established term "choked disc,"[1] for it is ex-

[1] The term is not entirely satisfactory, for though it implies stasis and swelling of the nerve-head it leaves retinal œdema and other changes, especially the degenerative ones, out of consideration.

In order to express both the "mechanical" and "inflammatory" processes in one term, Baas introduced the combination "*Stauungspapillitis*," and J. Herbert Parsons in his recent volume (The Pathology of the Eye, Vol. IV, 1908) strongly favors the term "papillœdema," which seems to have been used independently by Elschnig. This term has met with some favor, and has been used by George E. de Schweinitz and Halliday in a

pressive, and was introduced as an English equivalent for von Graefe's original designation *Stauungspapille*. There would be a further reason for its appropriateness could it be conclusively shown by experiment that all gradations of the process may represent the mechanical effects of increased intracranial pressure—and whether this leads primarily to venous stasis in the optic veins (von Graefe) or to cerebrospinal fluid stasis in the optic sheath (Schmidt-Rimpler and Manz) is of secondary consideration.

Before our experiments were undertaken, we must admit having been somewhat prejudiced in favor of a mechanical explanation, owing to rather an unusual experience with a long series of clinical cases, now embracing over four hundred instances of the condition we are pleased to call choked disc, many of the observations being difficult to explain on any other basis.

Briefly, these clinical observations may be divided into three groups. They have shown us (1) that the eye-grounds in most cases of cerebral trauma, often a few hours after the injury, show evidences of stasis, which may rapidly lead to œdema of a measurable height, first appearing on the nasal side of the disc. The increase of pressure may not necessarily be due to a large, actual extravasation of blood, as in apoplexy, but to a simple cerebral œdema consequent upon the minute extravasations of concussion or contusion.[2] In these cases the neuro-retinal lesion, which is indistinguishable from certain grades of so-called "optic neuritis," cannot possibly be due to other than the mechanical influence of increased intracranial tension, and it is well known that prompt operative relief from the pressure leads often to an equally prompt subsidence of the congestion and œdema of the nerve-head.

Further (2), owing to the frequent similarity between the condition seen in the eye-grounds of patients with tumors and of those in whom nephritis is accompanied by headache and vomiting, or other signs suggestive of increased intracranial tension, we have been led to believe that the process in the two conditions is largely of a common origin and due to pressure, which in the latter case results from cerebral œdema. Thus we have found that the neuro-retinal changes in nephritis—the so-called "*neuro-retinitis albuminurica*"—can often be temporarily modified, as Sänger has also observed, by a lumbar puncture which will disclose a superabundant fluid under tension; and what is more may be permanently modified by cerebral decompression. The same is true of many cases of cerebral arteriosclerosis when vascular disease has led to areas of cerebral œdema.

Finally (3), we have seen, in corroboration of the results of others, a great number of instances of partial or total subsidence of a choked disc after simple decompression.[1] This, more than any other factor, has served to favor a mechanical rather than a toxic source of the neuro-retinal change, which first or last is observable in most cases of cerebral tumor.

Experimental Observations.

Some years ago (1900) during the course of an investigation concerning the symptomatic phenomena of cerebral compression it was noted by one of us that the rhythmicalities of pulse-rate and blood-pressure, which were often brought out by a general increase of intracranial tension, produced after the method of Leonard Hill by letting fluid under pressure into the subdural space, were observable in the eye-grounds much as they were through the glass window inserted in the skull over a dural defect. In other words, a condition of venous stasis of cortex and retina was the first sign of vascular disturbance. When the pressure was gradually increased to a point equalling arterial tension, there occurred a compensatory rise in blood-pressure which was attributed to stimulation of the vasomotor center by the temporary bulbar anæmia. If, during this regulatory process, Traube-Hering waves were elicited, as was often the case, the retinal arteries would come into view as the arterial pressure exceeded the intracranial tension, and would disappear as the wave receded to fall momentarily to a lower level—and so on indefinitely.[4]

recent valuable paper (The Operative Treatment of Papillœdema, etc. Transactions of the College of Physicians of Philadelphia, 1908).

Though at first we were inclined to accept "papillœdema," this has seemed unwise on further consideration, for the term actually conveys nothing more of the process than does "choked disc," and its adoption would only add confusion, unless there were some understanding that the new term was expressly introduced to cover the entire process. This is not likely to occur since Parsons, on the whole, seems to be in favor of a mechanical origin of the lesion; whereas, Elschnig is emphatically opposed to any other than an inflammatory one.

Marcus Gunn's subdivision (British Med. Journ., Oct. 26, 1907) of the clinical stages of the lesion should be generally adopted, but with de Schweinitz we look with disfavor on his designation "tumor papillitis."

[2] This is true also of postoperative extravasations or œdema, and the sign is so valuable an indication of such an accident that it is our custom after all critical cranial operations not only to keep a continuous record of pulserate and blood pressure, but also to keep watch of the retina for early signs of a choked disc.

[3] Recent important contributions to this subject have been made by Eugene v. Hippel in Germany (v. Graefe's Archiv für Ophthalmologie, 1908, Bd. LXIX), by G. E. de Schweinitz in this country (Loc. cit.) and by Leslie Paton in England (Transactions of the Ophthalmological Society of the United Kingdom, 1905, Vol. XXV, and 1908, Vol. XXVIII). It is quite probable that Paton's studies of Sir Victor Horsley's cases at the National Hospital, before and after operation, will modify the view so widely held in Great Britain favoring the inflammatory origin of the lesion. It will be recalled that this view was stoutly supported by Sir William Gowers in his classic "Medical Ophthalmoscopy" (London, 1890, p. 78). A distinguished neurologist in this country has recently written (Boston Med. and Surg. Journ., February 1, 1906), "The toxic factor in the production of neuritis has long been recognized, and it is believed by many to be of importance in the production of headache, mental disturbances and other symptoms. Relief of pressure will, therefore, have little influence upon any symptoms of toxic origin."

[4] It is to be noted that this reaction of the laboratory experiments, called out by an acute increase in tension, is comparable only to the reaction in clinical cases which occurs with hæmorrhage or rapid œdema: it is not a characteristic of the long-standing or chronic increase of tension which occurs in cases of

At that time the observer's interest was directed chiefly toward the blood-pressure reaction, and for this reason, as well as from lack of familiarity with the picture of retinal œdema in the dog, the condition was overlooked.

In 1906, Eyster, working in Howell's laboratory, employed the same methods for the study of Cheyne-Stokes respiration, finding that during the period of blood-pressure elevation the stage of apnœa corresponded with the recession of the blood-pressure wave, the respiratory stage with its crest.[5] During the course of his experiments, some of which we attended, a high grade of choked disc was found to have been produced by this method of raising pressure. The observations, therefore, were repeated for the purpose of studying the retinal condition alone.

The method, which in principle is practically the same as that originally followed by v. Schultén and others, needs no especial description. With the animal under anæsthesia, a small trephine opening is made over the parietal eminence; the underlying circle of dura is cut away, and a snugly fitting canula is screwed into the cranial opening until its inner end is flush with the dura (Fig. 1). A long rubber tube connects this canula with a pressure flask, which may be raised or lowered and which contains normal salt solution at body temperature. A mercury manometer is inserted in the course of the tube for the purpose of recording the level of fluid pressure exerted against the brain. As Adamkiewicz has emphasized, fluid thus introduced passes out more or less freely from the cranial chamber, the escape taking place largely by way of the arachnoidal villæ directly into the large dural sinuses. This outflow, however, varies greatly in different experiments and even if considerable in amount affects but little the measured increase of tension.

A. The notes of two fairly typical experiments to show *the effects of an acute increase of tension from the subdural introduction of fluid* are as follows:

Observation IV.—December 6, 1905. Chlorotone and ether anæsthesia. Brown and white fox terrier.[6]

Atropin used to dilate pupils. Canula over left hemisphere; pressure with normal salt solution deeply stained with methylene blue. Examination of fundus shows nothing abnormal except in the left eye, where at lower edge of the disc a small patch of opaque nerve fibers is observed. The disc occupies the same plane as the retina. The veins and arteries are normal in size and color. No difference in condition apparent in the two eyes. Slight pressure on the eyeball completely obliterates the large veins on the optic disc.

2.38 p. m. Fluid allowed to enter cranial chamber with a pressure of 20 mm. Hg.

2.50 p. m. *Left eye:* Veins tortuous and disc swollen 2 D. under inferior temporal vein. *Right eye:* No changes beyond filling of veins, the small vessels showing a distinct increase in size.

2.58 p. m. Pressure raised to 30 mm. Hg. with resulting increase in tortuosity of the veins. Pulsation of veins noted at this stage.

3.06 p. m. Distinctly swollen right disc. No blue color showing in either eye.

3.25 p. m. By this time there has occurred a definite swelling of both discs without any further increase in the size or tortuosity of the veins since the last note.

3.35 p. m. A definite exophthalmos of both eyes, with dilatation of conjunctival veins, has occurred.

3.48 p. m. By compressing the eyeball it is possible to reduce the swelling of the disc in the right eye and to bring veins back to normal proportions. The disc has not increased in height on the left side.

4.03 p. m. On liberating right eye from external digital pressure exerted for several moments, some œdema is seen to have occurred in the conjunctiva. No change has appeared in the pupil of either eye.

4.18 p. m. Pressure raised to 40 mm. Hg. leads to dropping of fluid from the nose and to evident bulbar symptoms, so that pressure is discontinued.

Observation VI.—December 13, 1905. Chlorotone and ether anæsthesia. Fox terrier.

Atropin used to dilate pupils. Ophthalmoscopic examination shows hypermetropia of 2 D.; both retinæ normal; careful topographical study made of disc and vessels.

Canula inserted over left hemisphere, pressure flask containing warm normal salt solution deeply stained with methylene blue.

3.04 p. m. Fluid allowed to enter cranial chamber, pressure flask being slowly raised to level equalling 30 mm. of Hg. Distinct dilatation of veins; pulsation observed in veins.

3.07 p. m. Œdema commencing to appear in disc with no appearance of blue fluid: veins tortuous: edges of disc indistinct: height 3.5 D.

3.15 p. m. Retina has become œdematous and veins do not appear quite so large: height of disc 6 D.

3.18 p. m. Pressure increased to 55 mm. Hg.

3.28 p. m. A small hæmorrhage has occurred at upper margin of right disc, apparently the result of the giving way of a small venule.

3.48 p. m. Condition has remained practically unchanged, though patches of the disc seem to have a bluish tinge (?) as though stained by the fluid. 50 cc. of fluid has run in from pressure flask.

3.52 p. m. Pressure increased to 90 mm. Hg.

3.59 p. m. Moisture beginning to drip from nose. General appearance of fundus shows a deeper hue. As yet no outspoken change in pulse-rate or respiration.

4.05 p. m. Pressure suddenly raised to 140 mm. with temporary cessation of respiration, and convulsion. Pressure increased to 160 and then to 180 with periodic respiration and high-pressure vagus pulse. Pressure of 240 mm. of Hg. necessary to produce usual terminal phenomena of compression.

Autopsy.—Brain found deeply stained, particularly right hemi-

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brain tumor or hydrocephalus. Through failure to appreciate this, confusion has arisen in the minds of many clinical observers in regard to the blood-pressure readings of tumor cases, for in them a considerable increase of intracranial pressure need not elicit any striking rise in arterial pressure.

[5] J. A. E. Eyster, M. D.: Blood-Pressure Changes in Cheyne-Stokes Respiration. Johns Hopkins Hospital Bulletin, 1906, Vol. XVII, p. 296. Also Clinical and Experimental Observations upon Cheyne-Stokes Respiration. Journal of Experimental Medicine, 1906, Vol. VIII, p. 565.

[6] It may here be stated that in this, as in all other of the experiments, the animals were stupefied by the ingestion of a physiological dose of chlorotone before the administration of ether, and further that in all cases in which recovery from the anæsthetic was permitted, every effort was made, by the continuance of narcotics, to completely alleviate any possible discomforts, just as would be done with human beings suffering from comparable maladies.

sphere. No apparent œdema or blue staining of orbital tissues, though marked dilatation of all veins is present. No blue staining of frontal or ethmoidal sinuses. Brain not œdematous but stained a deep blue, particularly over the right hemisphere. Visible blue staining of cortical nervous system extends part way down the cord, but not beyond lower thoracic region. Both optic nerves deeply stained, and a distinct increase of fluid is apparent in Schwalbe's sheath. No trace of blue staining in abdominal or thoracic viscera.

The eyes were hardened in formalin and cut, showing, in spite of the shrinkage during fixation, a swelling of the disc which was definite though by no means as great as a height of 6 D. would indicate.

With the object of fixing the œdematous retinal tissues under the conditions of the experiment, so as to obviate in a measure the inevitable shrinkage of subsequent fixation, the above observations were modified by using 4 per cent. formalin instead of salt solution for the pressure fluid.

The results of an experiment of this kind may be briefly recounted. With the animal under anæsthesia the warmed formalin solution was allowed to enter as usual over the left hemisphere and was held at the constant pressure of 30 mm.

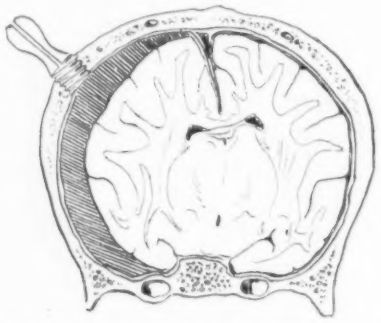

FIG. 1.—Sketch of coronal section of cranium to show dislocation of brain, in general-pressure experiment with methylene blue formalin. Fluid chiefly over left hemisphere, but tension presumably everywhere equal and eyes equally affected.

of Hg. In addition to the changes characterizing the experiments just detailed, an exophthalmos appeared on the contralateral (right) side soon after the pressure was exerted, and not until shortly before death did it occur on the side over which pressure was primarily being exerted.[7] Breathing continued nearly unaffected for an hour and a half, when a primary respiratory paralysis ushered in death.

The postmortem examination showed how, even when introduced into the free subdural space, the fluid need not find its way in equal amounts everywhere in the cranial chamber, though doubtless, from dislocation of the falx and hemisphere, apparent in this case (Fig. 1), the pressure effects may be transmitted everywhere equally. Sections were made of the eye and show (Fig. 2) well fixed the œdematous swelling of the nerve-head and distension of the sheath.

[7] In passing, it may be noted that in acute experiments of this type, with supposed "general pressure" from fluid, we have not infrequently seen the œdema of the disc and retina occur first in the opposite eye, to be followed later by equal changes in the near eye.

These observations, therefore, tend to confirm the experiments of Merz and Schmidt-Rimpler, the results of which were not corroborated by Kampherstein and Heine and have been most emphatically opposed by Adamkiewicz, who says:[8] "Künstliche Drucksteigerungen im Schädel bei Thieren niemals zu einer 'Stauungspapille,' sondern regelmässig nur zu Stauungen in der Venen der Chorioidea führen."

B. To determine *the effects on the eye-grounds of simple acute compression unassociated with the artificial introduction of fluid* but in which the fluid normally present plays an identical rôle, the following type of experiment was made:

OBSERVATION V.—December 8, 1905. Chlorotone and ether anæsthesia. Medium-sized, long-haired mongrel dog.

A one-inch trephine opening was made in the mid-line just anterior to the occipital protuberance, exposing longitudinal sinus and a portion of dura over each hemisphere.

The condition of the eye-grounds remained unaffected by this cranial operation. While pressure with the finger was being exerted against the exposed area of dura the ophthalmoscope showed first a filling of the larger veins and then the gradual appearance over the disc of small venules not before observable. Many of these smaller venules dilated to a considerable size, accounting for the hyperæmic appearance of the disc.

A few minutes of pressure sufficed to produce a swelling of the disc of 2 D.: a stronger pressure continued for some time increasing it to 7 D., with the associated characteristic appearances. On releasing the pressure the venous engorgement rapidly subsided and the small distended venules faded away. No change in the arteries was observed.

After an interval of five minutes strong pressure was reapplied and continued for twenty minutes, forcing the disc to a height of 7 D., and causing a marked œdema of the retina as well.

This neuro-retinal swelling, on again relieving the pressure, persisted for an hour, at which time a futile attempt was made to open the globe so as to directly observe the swelling, but this was unsatisfactory, from the local hæmorrhage.

C. A number of experiments of the type of A and B were then made, with the optic nerve itself exposed so that by direct observation *the effect of intracranial pressure on the vaginal sheath itself could be seen.*

OBSERVATION XI.—January 3, 1906. The experiment was conducted as in type A, with the usual preliminaries and the canula introduced over the left hemisphere. Salt solution deeply stained with methylene blue was used for the pressure fluid.

After making a number of the usual pressure observations the flask was lowered to zero level and a lateral orbital exposure made by continuing the scalp incision forward and around the eye. On removing the soft parts from the orbit and temporal fossa the globe and nerve were isolated back to the optic foramen.

The pressure flask was then raised to 30 mm. of Hg., with resultant filling of the sheath and visible enlargement of the ampulla. It was thought, too, that there was a palpable increase in intraocular tension. At the same time some of the veins over the globe (anterior ciliary), which had become divided in the operation, but which did not require ligation, began to bleed, others to distend and become tortuous behind their terminal thrombi. A systolic pulse was noted also in the sheath similar to that seen in the manometer during a pressure experiment

[8] A. Adamkiewicz: Zur Frage über das Wesen der sogen. "Stauungspapille." Neurologisches Centralbl. März 1, 1905, Bd. XXIV, p. 206.

when compression suffices to call out a strong vagus pulse with rise in arterial tension—a pulse, in the latter case, transmitted to the compressing fluid.

An exophthalmos of the unexposed eye occurred before death during some of the later observations, for there were many repetitions of the observation during the course of a few hours.

Autopsy.—The left hemisphere was blue-stained, with only a trace of coloring on the right, there being none in the right optic sheath. The left was faintly stained fairly well down toward the ampulla.

Similarly, other observations of the type B were made in which globe and optic nerve were isolated, but instead of introducing fluid to increase tension, digital compression was made on an exposed area of dura. In these cases, as in the above, the nerve sheath and ampulla would bulge coincidently with the rapidly forming œdema of the disc, the fundus being especially well seen in these cases, owing to the wide pupil. At the same time the vessels accompanying the optic sheath externally were seen to dilate and become markedly tortuous. The same thing was shown by the ophthalmoscope to take place in the retinal vessels, and in one instance the appearance of movement of the venous blood in the larger veins over the disc was observed—an appearance which can be best seen through a cerebral window during a certain stage of compression in which there is a tendency to flattening of the veins and which may, in this instance, have been indicative of the slightly increased intraocular tension which seemed to be present in these isolated globes.

During the course of the series of observations some casual efforts were made to determine whether the fluid distending the sheath in the two types of experiment was in the subdural or subarachnoid chamber. There is little doubt but that in most tumor cases the pent-up fluid is found, as might be expected, in the subarachnoid spaces, the distension of which in the neighborhood of the chiasm can be well seen in many cases of intracranial tension accompanied by choked disc, provided the brain is hardened in situ and a coronal section made through this region (Fig. 3). Similarly, in the choked disc of man not only can the distension be shown to be in the subarachnoid space on microscopic sections of the nerve (Fig. 4), but also if a window is made in the wall of a well distended ampulla in a case with choked disc of long standing, the thickened meshwork of the arachnoidal spaces can be well seen (Figs. 5 and 6).

Whether or not, when the fluid is introduced under the dura as in experiments of the type A, it passes into and distends the subdural space of the sheath we are a little uncertain. This would seem to be probable, from the study of certain cases in which the pressure fluid contained fine particles of animal charcoal in suspension or when India ink is used. Doubtless in the majority of clinical cases the distension occurs in the subarachnoid spaces where physiologically the fluid first appears, and with the exception of the various œdemas, traumatic and otherwise, the subdural space at operation usually is found comparatively dry (Figs. 7 and 8).

It is apparent from these first observations that *a neuro-retinal œdema with marked elevation of the papilla may accompany conditions which raise intracranial pressure whether from the introduction of new fluid under tension or from transmission of tension to the fluid already present;* and, furthermore, *that coincident with* (possibly antecedent to) *the production of the neuro-retinal change there will occur a visible distension of the optic sheath.*

This being established an effort was made to determine in how far venous stasis alone was capable of producing the lesion under investigation.

D. Experiments of the following type were undertaken in the attempt to determine *the effects of venous stasis alone.*

OBSERVATION II.—November 3, 1905. With an animal under anæsthesia and a simple blood-pressure band of the Riva Rocci pattern encircling the neck the pressure in the band was raised to 85-90 mm. of Hg. With this degree of pressure a distinct widening occurred, particularly in the smaller retinal veins. With further increase in the pressure the dilatation affected the larger vessels, which became slightly tortuous. However, even with a long standing pressure of this kind, slightly below arterial pressure, and in spite of the marked passive congestion of the extracranial tissues, the evidences of stasis in the eye-grounds not only did not increase to the point of causing œdema but in the course of time the congestion actually subsided.

The conditions here were comparable to the similar experiment made on man (on the person of one of us),* although naturally in this case the pressure could not be so long continued. In other words, evidences of stasis alone, not reaching a degree sufficient to cause extravasation of fluid into the retinal tissues, resulted from cervical compression, and it was thought in the case of the dog that the large venous sinuses passing into the spinal canal sufficed to carry away enough blood to permit the total obstruction of the four cervical jugulars.

The experiment was given a more severe test with an animal kept for twenty-four hours under profound chlorotone anæsthesia and with an elastic tourniquet passed under the isolated trachea and tightly bound around the remaining cervical structures. This led first to a marked distension of the extracranial veins, especially well seen in the conjunctival and anterior ciliary vessels; also to some lachrymation, a stasis exophthalmos, and a temporary slow vertical nystagmus. The retinal veins became large and tortuous and an extravasation occurred in the deep tissues of the left retina. The arteries remained full, supposedly owing to their vertebral supply. In the course of an hour, however, the distension of the retinal veins and the exophthalmos disappeared, no choking of the disc or œdema of the retina having occurred in the interval. Eighteen hours later the eyes showed no change, though there was considerable œdema of the extracranial tissues headward to the band.

A further modification of these stasis observations was made during the course of the experiments of the type C with an isolated globe and optic nerve. When a delicate constricting

* The Blood Pressure Reaction of Acute Cerebral Compression, Illustrated by Cases of Intracranial Hæmorrhage. A Sequel to the Mütter Lecture for 1901. American Journal of Medical Sciences, June, 1903, Vol. CXXV, n. s., p. 1017.

band was placed near the optic foramen, around the exposed nerve, and tightened to a point just short of shutting off the central artery of the retina, this would lead to the usual ophthalmoscopic picture of stasis, but we were never able to cause an appreciable swelling of the disc or retinal œdema thereby.

Experiments of this type, therefore, showed us that *simple stasis in the retinal veins fails to produce anything more than the condition of venous engorgement which accompanies a choked disc* and never leads to a definite œdema of the papilla.

We recognize the fact that these observations are not entirely conclusive, that there are many things which deserve repetition, and that a different result might be obtained in eyes of other species than the dog. They do not serve to finally eliminate venous stasis as a primary factor in the production of choked disc, though the comparative ease with which the condition is produced by cerebrospinal fluid stasis and the difficulty with which it is produced by venous stasis indicates what in all probability is the essential element.[19]

E. Attempts were then made by observations of longer duration *to reproduce the histological alterations in the disc which characterize the long standing choked disc of tumor in man.*

Observation XVI.—April 14, 1908. A bilateral cranial defect with removal of a considerable area of bone under each temporal muscle had been made three weeks previously. At that time the dura had been opened and the pyramidal tract on each side divided for purposes of studying the resultant Wallerian changes. The patient—a medium-sized mongrel dog—had made a perfect recovery and the wounds had healed by primary union.

It was found that slight pressure exerted against the temporal muscles over the defects led to a drowsy state, without appearing to occasion any discomfort, just as is true of man when pressure is made over a large cranial defect. On continuance of the pressure for some minutes the eye-grounds, which previously were normal, showed a swelling of the discs amounting to 2 D. (comparable to experiments of the type B).

A head bandage of crinoline was applied with pads over the defects so as to keep up a moderate degree of pressure, and morphia was administered to assure us of the animal's being kept in a stuporous state.

April 15. A bilateral swelling of each disc of 3 D. was present.

April 18. Condition unchanged.

April 20. A considerable increase in the swelling on the left, with definite retinal œdema. Two small hæmorrhages following the line of the lower veins. Right eye unchanged.

May 9. No further clinical alterations have been observed in the eyes. Animal sacrificed on this day: the pressure having been continued most of the time during the period of three weeks, it was thought that permanent histological changes would be apparent in the nerve.

Autopsy.—Brain, which had been hardened in situ by carotid injections of formalin, showed considerable flattening over each parietal lobe. No unusual dislocation of cerebellum into foramen magnum was observable.

Eyes were hardened in Zencker's fluid. The optic sheaths did not seem to be especially distended.

Histological examination showed swelling of the disc and marked separation of the tissues of papilla and retina by œdema (Figs. 9 and 10). There were numerous small extravasations of blood, and beginning round-cell infiltration was apparent.

Though the changes were not particularly advanced, the evidence in the neuro-retinal structures was sufficient to show the tendency toward the profound alterations in the eyes which are found in cases of long standing pressure.

F. A number of experiments were finally made by *the introduction within the cranium of a foreign body with the object of more closely simulating the conditions present in tumor.*

The first attempts in this direction were made with melted paraffine introduced from a warmed Pravatz syringe directly into the cerebral or cerebellar substance through a small opening drilled through the bone. Though certain temporary retinal changes occurred in a few instances, particularly after some of the cerebellar injections, the neuro-retinal disturbance was but transitory and the solidified mass of paraffine was tolerated without further effect on the brain beyond that occasioned by the immediate local destruction of tissue. We appreciated, therefore, that some foreign substance which would exert a constant elastic pressure was essential, and it was found that fragments of compressed sponge-tent were admirably suited to this purpose.

Observation XX.—December 15, 1908. 2 p. m. Under ether, and with painstaking surgical precautions, the left occipital base was exposed by Dr. G. J. Heuer, and a small 6 mm. trephine opening made without dural injury. Through this opening the dura toward the mid-line was separated from the bone and four or five fragments of dry sponge-tent were introduced. The wound was then closed.

3.45 p. m. A horizontal nystagmus is present in both eyes, more marked in right than left. The fundus, which was normal before and immediately after the operation, now shows a distinct œdematous elevation of the upper part of the right disc with marked engorgement of the veins. Left eye normal.

5 p. m. No further change; nystagmus has disappeared. Patient has recovered from anæsthetic and though somewhat ataxic is lively and running about.

December 16, 3 p. m. General condition excellent. Marked venous engorgement of both eyes with œdema on the right persisting, though not increased. Pupils normal.

December 17, 3 p. m. Somewhat apathetic and unresponsive. Distinctly ataxic and unsteady when on feet. *Right Eye:* Venous engorgement with distinct swelling of entire disc. *Left Eye:* Engorgement and general haziness of disc from low grade œdema.

December 21. The condition noted above has persisted unchanged until to-day. Venous congestion much less marked in both eyes. Disturbance of gait disappearing.

[19] It should be noted in this connection that stasis such as occurs in cases of sinus thrombosis, especially of the widespread autochthonous form, is usually associated with pressure phenomena and a high grade of choked disc. Here the venous stasis, of course, plays the primary rôle, but it leads to definite pressure symptoms, doubtless with an increase in the tension of the cerebrospinal fluid around the base of the third ventricle and a consequent distension of Schwalbe's sheath. Whether this distension of the optic sheath is what leads to the stasis in the retinal veins, as some have thought, or whether the stasis is due to compression of the cavernous sinus (v. Graefe) or other outlets for the blood still nearer the heart can at present be only conjectured.

It may be noted further that we did not succeed in reproducing in the dog the choked disc of man which follows cerebral trauma, either from difference in character of intracranial circulation or because of inconsequent methods.

FIG. 2.—Section of canine nerve and retina, to show experimental choking of disc; also optic sheath distended by blue-stained fixative fluid and a certain amount of blood.

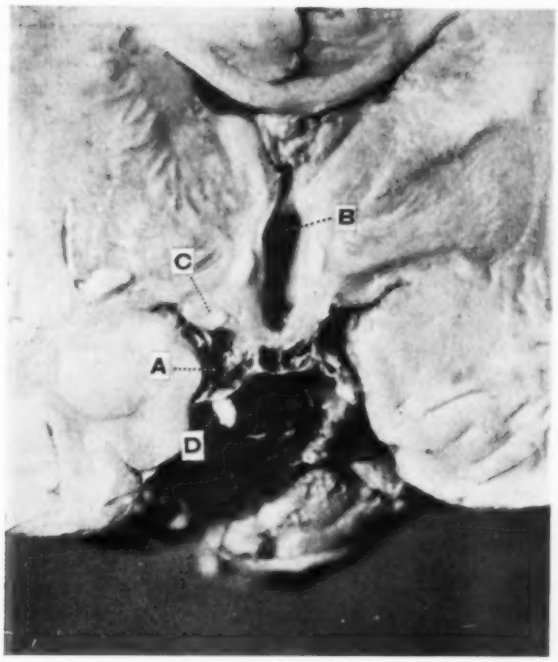

FIG. 3.—Cerebrum of patient with subtentorial tumor causing a low grade of hydrocephalus and choked discs in the atrophic stage. Brain removed after hardening in situ. Coronal section passing through interpeduncular space. Note (A) the distension of the subarachnoid spaces of this region; (B) slight widening of third ventricle; (C) optic tract; (D) oculomotor nerve.

FIG. 5.—Showing marked ampullaform distension of Schwalbe's sheath in a case of long standing choked disc. Note the thickened bands of the subarachnoid spaces, exposed by reflecting a window from the dural sheath.

FIG. 4.—Section through the centre of the nerve and papilla in a case of long standing choked disc accompanying cerebral tubercle; distension of Schwalbe's sheath limited to subarachnoid spaces.

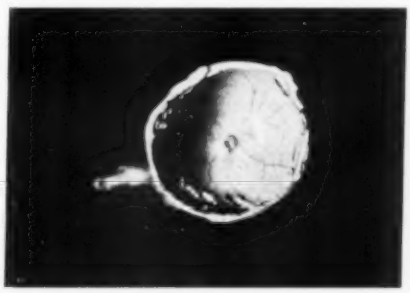

FIG. 6.—Same eye as in Fig. 5, looking directly into fundus. Note projection of disc especially marked on nasal side, *i. e.*, away from macula. Note also tortuosity of veins.

FIG. 7.—Section of nerve and papilla from a case of acute choked disc (two weeks) in a patient who succumbed to pressure from cerebral œdema. Note ampullaform dilatation of Schwalbe's sheath, the fluid being confined to the subarachnoid spaces and leading to rupture of many of the delicate sub-arachnoidal bands.

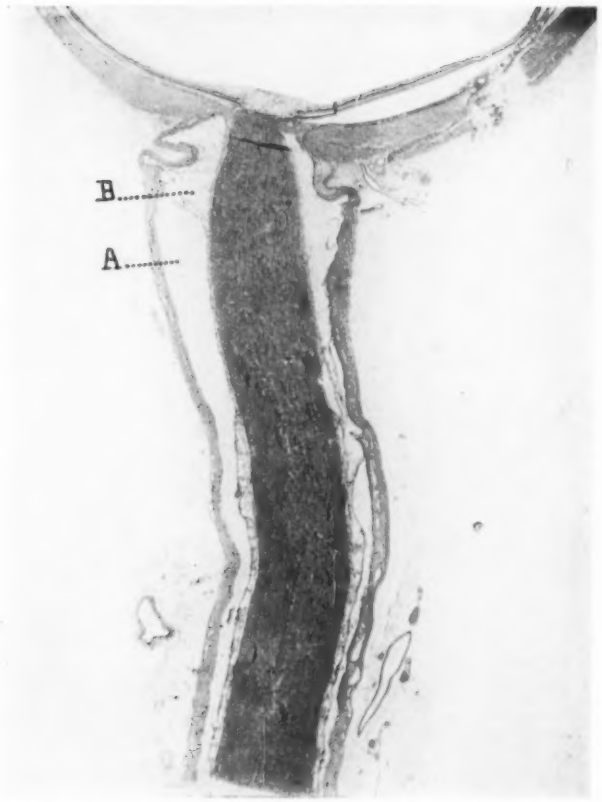

FIG. 8.—For comparison with Fig 6. Nerve and edge of disc from a similar case. Note ampullaform dilatation of sheath enfolded during fixation; distension by fluid in subdural space (A), as well as in subarachnoid spaces (B).

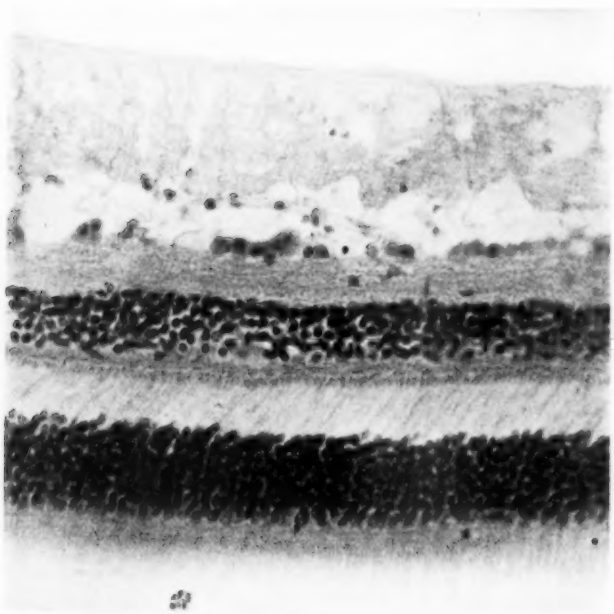

FIG. 9, *Observation XVI.*—Showing marked separation of retinal tissues by œdema, in this field practically limited to the nerve fiber layer. Note destruction of ganglion cells, as well as a marked lengthening and tortuosity of nerve fibers.

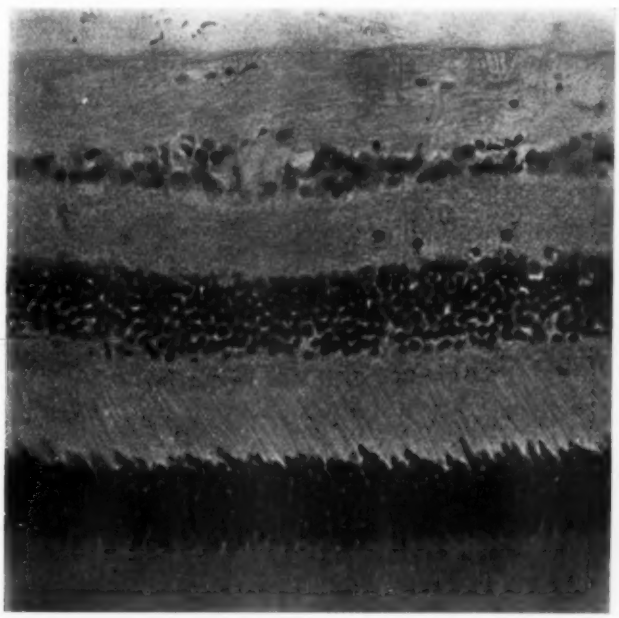

FIG. 10.—Section from a practically normal eye to contrast with Fig. 9.

FIG. 11, *Observation XX.*—Showing position of partly organized sponge over left cerebellum (cf. Fig. 12).

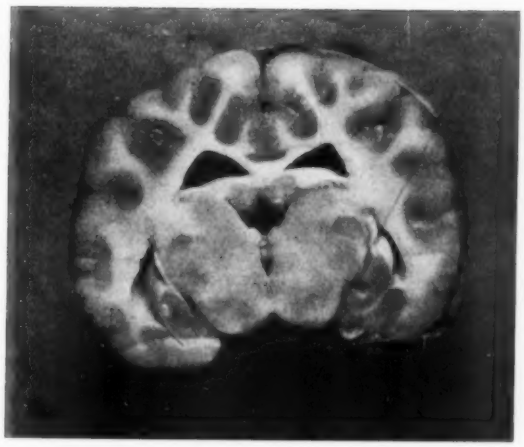

FIG. 12.—Coronal section of cerebrum, *Observation XX*, showing ventricular distension from moderate grade of obstructive hydrocephalus (cf. Fig. 11).

FIG. 13.—Showing brain, optic nerve and eyeball from *Observation XXI.* Note position of partially organized sponge and distension of optic sheath.

FIG. 14.—Cross-section of brain in *Observation XXI*, to show extent of pressure dislocation exerted by the tumor-like foreign body (cf. Fig. 13).

December 29. All evidences of neuro-retinal change have disappeared. No cerebellar symptoms. Wound has healed perfectly.

January 2. Eyes remain practically normal. Chloroformed.

Autopsy.—Brain and eyes hardened in situ. A moderate degree of compression of left cerebellum by swollen fragments of sponge (Fig. 11), which on their dural aspects are adherent in a mass and are undergoing organization. No evidence of any local infection. A low grade of internal hydrocephalus is present (Fig. 12), sufficient, one would have supposed, to perpetuate in the retina some evidence of stasis at least, but this, if present, was unobserved. No particular evidence of swelling in Schwalbe's sheath.

OBSERVATION XXI.—December 15, 1908. 4 p. m. An operation was performed similar in technique to that recorded in Observation XX, but with the introduction of larger fragments of sponge-tent between bone and dura over the left hemisphere.

5 p. m. Fifteen minutes after closure of wound. Both eyes show marked tortuosity of retinal veins with practically no change in the arteries. Pupils dilated *ad maximum*. Practically no response to light. No nystagmus. No evidence of œdema of disc.

December 16, 3 p. m. Patient made a good recovery from the anæsthetic. Has taken food and drink, and though somewhat dull, is lazily moving about. Pupils normal in size and reactions. *Right Eye:* Upper portion of disc shows marked swelling and particularly in that direction there is extreme tortuosity and distension of the veins. *Left Eye:* The entire disc is clouded and distinctly swollen; veins enormously engorged and tortuous—much more so than on the right. No hæmorrhages. No exudates.

December 17, 3 p. m. Animal still dull and stupid. Both discs have increased in height.

December 18, 3 p. m. A still further increase in the swelling of both discs. The change is still particularly marked in the left eye, where great tortuosity of the veins persists.

December 29. The condition of the eyes remains practically unaltered, though the animal has largely recovered from his stuporous state and is more lively and responsive. The wound has completely healed.

January 2. Choked disc persists, more marked on left than right. Chloroformed.

Autopsy.—Brain and eyes hardened in situ by carotid injections of 10 per cent. formalin. Area occupied by fragments of elastic tent, which by process of organization are adherent to the dura though not to the overlying skull, is shown in Fig. 13 of upper surface of brain, and on section in Fig. 14. No internal hydrocephalus. No infection. Considerable distension of Schwalbe's sheath in both eyes (Fig. 13).

Histological examination shows marked œdema of neuro-retinal tissues and beginning round-celled infiltration.

It is our intention to make further observations of this sort with the intracranial introduction of sponge-tent, particularly as it may serve to throw light on the incidence of choked disc accompanying supratentorial and infratentorial growths, especially when in the latter case there is an associated hydrocephalus. It will be readily seen from the short notes upon these two cases that there are a number of points which need further elucidation, but for the purposes of this immediate report these two observations suffice to show that without the association of any toxic or inflammatory condition, it is possible to simulate experimentally the swelling of the nerve-head and the other retinal changes which characterize at least the early stages of choked disc in human patients.

To summarize the results of these experiments it may be said:

(1) That the introduction of fluid under tension into the intracranial subdural space will produce an acute œdematous swelling of nerve-head and retina—in other words, a choked disc—which can be observed during life with the ophthalmoscope and demonstrated by a study of the tissues after death.

(2) That simple digital compression exerted against an area of the dura exposed by a trephine opening and without the introduction of new fluid under tension will produce similar lesions.

(3) That these acute œdemas of the nerve-head and retina are associated, under both conditions, with distension of the optic sheath, particularly of its subarachnoid spaces.

(4) That venous congestion does not seem capable, without the concomitant action of fluid under tension in the optic sheath, of producing more than the congestive features of choked disc; in other words, under the conditions of the experiments it failed to occasion any appreciable œdema of the nerve-head.

(5) That long-continued pressure against a dural defect can lead to retinal hæmorrhages and other clinical, as well as histological, features which characterize chronic choked disc in man.

(6) That the introduction between the skull and dura of foreign bodies which are capable of subsequent increase in size and which possess some elasticity, will closely simulate the action of a new growth, and, placed either above or below the tentorium, will lead to the production of choked disc.

It may, therefore, be stated in conclusion:

(1) That the occurrence of the neuro-retinal œdema is primarily dependent on the passage of cerebrospinal fluid under tension from the subarachnoid spaces of the interpeduncular region into the vaginal sheath of the optic nerve, and that cerebral decompression often allows the process to subside, owing to a resultant diminution of tension from release of the confined fluid.

(2) That the experimental work corroborates many of the more recent clinical observations in showing that a choked disc, even of considerable height, may be rapid in its formation and, provided it has not gone on to the stage of new tissue formation, may rapidly subside; and thus speaks strongly in favor of a mechanical, as opposed to a chemical or inflammatory origin for the lesion.

INDEX TO VOLUMES 1-16 OF BULLETIN.

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ON THE EXCRETION OF HEXAMETHYLENAMIN (UROTROPIN) IN THE CEREBROSPINAL FLUID AND ITS THERAPEUTIC VALUE IN MENINGITIS.

By S. J. Crowe, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

In a previous publication[1] dealing more particularly with the excretion of urotropin in the bile and pancreatic juice, attention was called to the fact that after ingestion urotropin also appears in the cerebrospinal fluid.

As recorded at that time, the patient on whom this observation was first made was a boy, thirteen years of age, in whom a cerebrospinal fistula had occurred after a suboccipital operation for a cerebellar tumor, in consequence of the sloughing corner of one of the skin flaps. The discharging fluid soon became purulent; the temperature ranged between 100° and 103° F.; and as a fatal meningitis is the usual outcome of infected cerebrospinal fistulas of this nature, a like result was feared in this case.

Acting on the suggestion of Dr. Cushing, that urotropin might be excreted through the cerebrospinal fluid as well as through the bile and pancreatic juice, the boy was given a 10-grain dose of urotropin by mouth, and a few hours later some of the escaping cerebrospinal fluid was collected and examined. A chemical test showed that the drug was present in considerable quantity. Accordingly the dose was increased to 30 grains a day, diluted with large quantities of water. The immediate effect was not marked, as the temperature and the character of the discharging fluid showed no decided change during the following week. But after this the temperature slowly fell to normal, and the cerebrospinal fluid, escaping through the fistula, gradually lost its purulent character and became less in amount, so that three weeks after the administration of the first dose of urotropin the patient's temperature had reached normal and the fistula had entirely closed.

The finding of urotropin in the cerebrospinal fluid in this case led us to make further investigations of the subject.

Thus in cases of chronic nephritis, brain tumor or hydrocephalus, when lumbar puncture was to be performed, the patients were given a preliminary 10- or 15-grain dose of urotropin, and the cerebrospinal fluid after removal was tested by a modification of Hehner's test.[2] In all of these cases the chemical test was positive, showing that urotropin, after its administration by mouth, invariably appears in the cerebrospinal fluid. It may be added that a number of observations were made showing that the drug may possibly be as readily absorbed after rectal administration as when given by mouth.

In some instances the urotropin was not given until the cerebrospinal fluid was dripping steadily from the needle, and, by testing specimens every few minutes, the first appearance, maximum concentration and gradual disappearance of the drug could be easily followed. These factors naturally were found to vary somewhat with the individual and with the quantity of the drug taken, but in general, after a 15-grain dose of urotropin, the maximum concentration seemed to be reached after a period of from 30 minutes to one hour. This can readily be shown by the varying intensity of the amethyst color produced by the chemical test. If, after a 15-grain dose of urotropin, cerebrospinal fluid in 10-drop amounts be collected in a series of small test tubes at intervals of 5 minutes, and the reagent mixed with each, a very faint amethyst color will appear in one of the early tubes, growing more intense in the succeeding ones, and finally fading until its complete disappearance.

To determine whether the urotropin administered in therapeutic doses, appears in the cerebrospinal fluid in amounts sufficient to be of decided bactericidal value, observations were made on its inhibiting effect on the growth of organisms inoculated in the fluid after its removal from the body. The following investigation was made of the fluid withdrawn by lumbar puncture from a patient with hydrocephalus, in whom, for certain diagnostic purposes, a long continued escape of the fluid was permitted. While the cerebrospinal fluid was dropping at a steady rate the patient was given 45 grains of urotropin by mouth. Before the administration of the drug 5 cc. of the cerebrospinal fluid had been collected in a sterile test-tube; after its administration four specimens of like amount were collected at intervals of 30 minutes. Each tube was then inoculated with one loop from a 24-hour culture of streptococcus pyogenes, and incubated at 38.5° C. Twenty-four hours later a series of agar plates were made, taking one loop from each tube of cerebrospinal fluid. The results are tabulated in Table I.

In order to study the effect of urotropin administered in artificially produced meningitis, the observations were then

[1] On the Excretion of Hexamethylenamin in the Bile and Pancreatic Juice. The Johns Hopkins Hospital Bulletin, 1908, Vol. XIX, p. 109.

[2] This test is made as follows: To the clear cerebrospinal fluid a drop or so of milk or a very small amount of casein is added, and this mixture is stratified with an equal volume of the reagent, which is composed of 100 cc. of 99 per cent sulphuric acid and one drop of a 3 per cent ferric chloride solution. The sulphuric acid decomposes the urotropin into formaldehyde and ammonia, and a deep amethyst color develops at the juncture of the layers. If formaldehyde (urotropin) is present in too great a concentration, however, the color reaction may not occur without dilution of the fluid.

transferred to animals, the first few experiments being conducted on rabbits.

A very virulent organism was obtained by lumbar puncture from a patient who succumbed to a streptococcus meningitis. This organism was used throughout the entire series of experiments, its virulence being retained by its occasional passage through a rat. Only five observations were made on rabbits, of which the following will serve as a type:

TABLE I.

Lumbar puncture 9.30 a. m. Steady flow of clear cerebrospinal fluid.

Tube No.	Time a. m.	Inoculated with	After 24 hours' incubation.	Stained smear shows	Plates (compare photographs).	Number of colonies on plates after 48 hours' incubation.
I.	9.35	1 loop streptococcus.	Very turbid.	Abundant organisms.	Agar inoculated with 1 loop and plate made.	Very thick. Estimated number, 30,000.
	9.40	Patient given urotropin gr. 45 by mouth.				
II.	10.00	1 loop streptococcus.	Turbid.	Abundant organisms.	.....Do.....	Not so thick as in No. I. Estimated number, 20,000.
III.	10.20	.....Do.....	Slightly turbid.	Scattered organisms.	.....Do.....	Estimated number, 1,000.
IV.	11.00	.....Do.....	Slightly turbid on shaking.	Very few organisms.	.....Do.....	Estimated number, 800.
V.	11.30	.....Do.....	.....Do.....	.....Do.....	.....Do.....	Estimated number, 500.

Two animals of about the same size and weight were selected, and a small hypodermic needle was introduced into the lumbar subdural space of each. After obtaining a drop or two of cerebrospinal fluid, an equal amount of a bouillon culture of the organism was injected and the needle withdrawn. By means of a stomach tube 10 grains of urotropin was given to one of these animals immediately following the inoculation, and the dose was repeated at intervals of four hours. The other animal served as the control, receiving no urotropin.

Due to the virulent strain of the organism used and the great susceptibility of these animals to infection, both the inoculated animal and the control rapidly succumbed to a purulent meningitis. The animals receiving urotropin usually died on the third or fourth day, but the control animals invariably succumbed in less than 36 hours after the inoculation. The clinical symptoms, such as retraction of the neck and general muscular rigidity, were equally marked in both, but their onset was distinctly deferred in the animal receiving urotropin. The autopsy findings were identical; cultures and smears from the purulent cerebrospinal fluid showed an equal number of organisms in both animals.

TABLE II.

Observation VIII.—Showing the effect of urotropin administered by mouth on streptococcus meningitis in dogs.

Animal No.	Inoculated with 24-hour bouillon culture of streptococcus.	First dose of urotropin given.	Amount of urotropin given during 24 hours.	Clinical course.	Autopsy findings.—Microscopic smears and cultures.
I.	0.1 cc. injected under dura.	Control. No urotropin.	None.	Died 24 hours after inoculation.	Purulent meningitis. Smears and cultures showed abundant organisms.
II.	.....Do.....	Urotropin gr. 10 1 hour after inoculation.	30 grains.	Died on 2d day after inoculation.	Purulent meningitis. Smears and cultures showed abundant organisms.
III.	....Do.....	Urotropin gr. 15 immediately after inoculation. Animal still under anesthetic.	45 grains.	Died on 2d day after inoculation.	Purulent meningitis. Smears and cultures showed abundant organisms.
IV.	.....Do.....	First dose of urotropin (10 gr.) given 12 hours before inoculation, and repeated every 4 hours.	80 grains.	2d day—Very sick; refuses to eat; slight rigidity of neck and legs. 3d day—Much better; drank some milk. 4th day—Improving steadily; rigidity much less marked. 5th day—Continues to improve; given 2 to 3 liters of water a day with stomach tube. Continues to improve: apparently well. General neuritis suddenly developed on 15th day, and animal was sacrificed.	Cerebrospinal fluid clear; slight thickening and cloudiness of membranes around base; smears showed no organisms; cultures sterile.

Similar observations were then attempted on dogs, but owing to the great difficulty of making lumbar punctures on these animals it was necessary to resort to an operative exposure of the meninges. A number of experiments were made, the general results of which can be illustrated by a single series. Four animals, all perfectly healthy and of about the same size and weight, were selected. Under ether anæsthesia and with painstaking surgical precautions, they were serially inoculated in the following manner:

The back of the head and neck was shaved and the skin cleaned with alcohol, ether and bichloride. A median incision, about 10 cm. in length, was made tailwards from the external occipital protuberance. The muscles were separated, exposing the prominent spine or comb of the second cervical vertebra which, projecting upward, overlies the broad posterior arch of the atlas. On removing the upper two-thirds of this spine and strongly flexing the animal's head a small trephine opening was readily made in the posterior arch of the atlas. The dura was thus exposed without injury, and by means of a curved hypodermic needle and an aspirating syringe, cerebrospinal fluid could be withdrawn or organisms introduced into the subdural space with but little subsequent leakage or chance of infection of external tissues. (The external wound was never found infected.) The muscles and skin were then closed by interrupted stitches of black silk.

Each of the four animals mentioned above were inoculated with an equal amount of bouillon culture of streptococcus. One served as a control, the three others receiving urotropin under varying conditions and in varying amounts. The results are presented in tabular form in Table II.

All four of these animals, therefore, were inoculated with an equal amount of a very virulent culture of streptococcus, and although the second animal was given urotropin, the first dose was not administered until one hour after the inoculation had been made. The third animal was given the first dose immediately after the inoculation but while still under the anæsthetic. Both of these animals (II and III) lived but a short time longer than the control, and the postmortem findings and cultures were in every way similar in all three cases. Subsequent observations have shown that but very little urotropin is absorbed from the stomach of an anæsthetized animal, so that it was probably some time before the drug reached the acutely infected fluid. The fourth animal, as can be seen, made an apparently complete recovery, but was sacrificed, owing to the onset of symptoms of a painful neuritis; the autopsy showed the meninges to be sterile, and there were but slight traces evidencing past infection.

Although we have no accurate method of quantitatively testing the fluids for the amount of urotropin present, the impression has been gained, from the comparative color tests of cerebrospinal fluid and urine in these animals with an infective meningitis, that a larger amount of the drug appears in the cerebrospinal fluid under these circumstances than in the urine, where, under normal conditions, the greatest amount is found. If this prove to be true it would suggest that some selective action may occur, possibly through the agency of the leucocytes, which have the power of taking up the drug, as Vindevagal[3] has shown by an examination of these cells washed free of serum.

Only a few of the forty experimental observations which we have made have been cited in this report, but they serve to illustrate that animals that have received several doses of urotropin before the cerebrospinal space has been inoculated with pathogenic organisms will, even if recovery does not actually take place, survive longer than animals that have received the urotropin after the inoculation, and much longer than those to whom none of the drug has been administered. It has been our impression that, in case the first dose of urotropin was given subsequent to the inoculation, the progress of the infection was merely held in abeyance during the continuance of subsequent active therapy, and that as soon as the drug was withdrawn the organisms immediately began to multiply with a return of clinical symptoms. This is much the same experience that has long been had with urotropin administered in genito-urinary infections, and it is also akin to our experiences with the drug in infections of the biliary tract. It would seem, therefore, that the most marked therapeutic value of the drug would be for prophylaxis or at least for cases of early infection.

During the past year it has become a routine measure in the Johns Hopkins Hospital to promptly administer urotropin to all patients with lesions that not infrequently are followed by infection of the meninges; and owing to the complete absence of such a complication in quite an extensive series of cases, the prophylactic importance of the drug seems fairly well demonstrated. This series includes a number of instances of compound fracture of the skull, of gunshot wounds of the head, and of patients with cerebrospinal fistulæ, under the daily administration of from 30 to 60 grains of urotropin. Its use has also been further extended as a preliminary to the performance of ventricular or lumbar puncture, in case the local conditions are such as to make possible the inoculation of the meninges with organisms from an infected skin; in the same way the preliminary taking of urotropin is desirable before a first catheterization or one necessitated in the presence of an urethral infection. It is possible, too, that the drug might wisely be used in cases of extracranial infection when extension to the meninges is feared, as in infected wounds of the scalp, otitis media, or suppurations of the cranial sinuses. Its administration might further be desirable in elaborate spinal or cerebral operations, in view of the possible, though fortunately rare, slips in aseptic technique which may occur in these cases.

Summary.

(1) Urotropin, when given by mouth, invariably appears in the cerebrospinal fluid. This fact has been demonstrated by a large number of observations on man, and is also true for dogs and rabbits.

(2) The largest amount of urotropin is present in the

[3] Annales de la société royale des sciences médicales de Bruxelles, 1902, Vol. II.

PHOTOGRAPHS OF PLATES I, III, IV AND V, DESCRIBED IN TABLE I.

Fig. 1, Plate I.—Showing innumerable minute colonies; estimated number 30,000. Result of inoculation of fluid removed before urotropin was given.

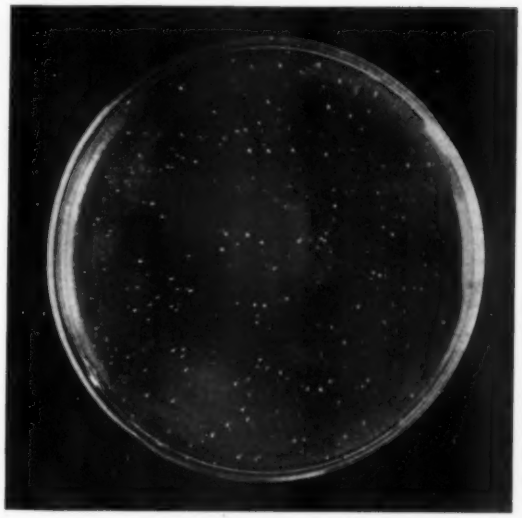


FIG. 2, Plate III.—Showing many larger colonies, though total number only about 1000. Result of inoculation of fluid removed forty minutes after urotropin.

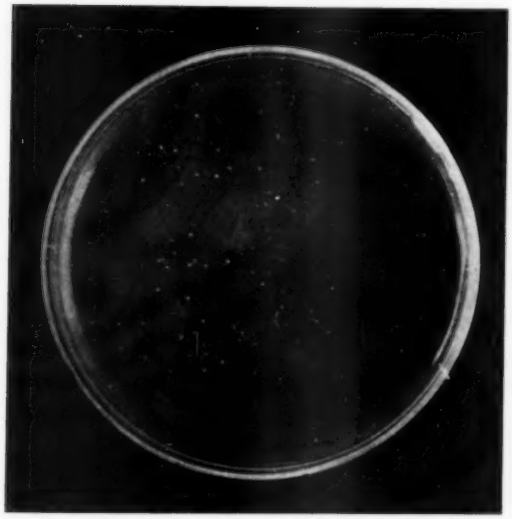


Fig. 3, Plate IV.—Estimated number of colonies, 800. Result in fluid removed one hour and twenty minutes after inoculation.

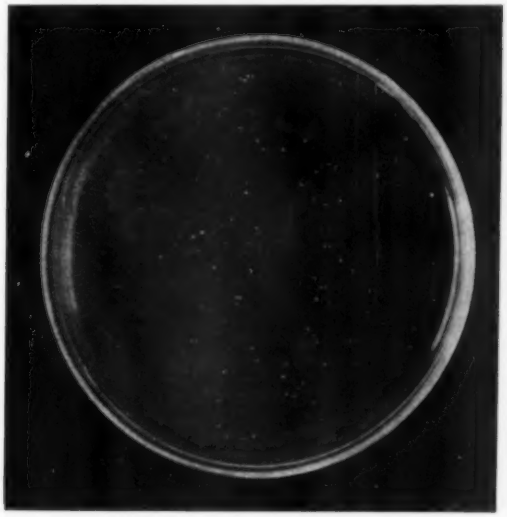


Fig. 4, Plate V.—Approximately 500 colonies. Result in fluid removed one hour and fifty minutes after inoculation.

cerebrospinal fluid from 30 minutes to an hour after the ingestion of the drug.

(3) After doses of urotropin, within therapeutic limits, a sufficient amount of the drug appears in the cerebrospinal fluid to exercise a decided inhibitory effect on the growth of organisms inoculated into this fluid after its removal from the body.

(4) Following a subdural inoculation of dogs and rabbits with streptococcus, 60 to 80 gains of urotropin a day, given under conditions which insure absorption, will markedly defer, and in some cases prevent, the onset of a fatal meningitis.

(5) In view of these observations, the prompt administration of urotropin is advised in all clinical cases in which meningitis is a possible or threatened complication, or even when meningeal infection has actually occurred.

IS THE PITUITARY GLAND ESSENTIAL TO THE MAINTENANCE OF LIFE?[1]

By Lewis L. Reford, M. D., and Harvey Cushing, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

Of late years the symptom-complex of a number of maladies which are frequently associated with tumors or hypertrophies of the pituitary gland has become fairly well determined, this being particularly true of acromegaly, of gigantism, and of what is known in Austria as Frölich's disease—a condition characterized by sexual infantalism and an increase of panniculus. When the altered configuration of the pituitary fossa due to the glandular enlargement can be objectively demonstrated by a radiogram, the existence of the concomitant hypophyseal lesion can be assured.

In addition to the peculiar constitutional disturbances which accompany many of these hypophyseal growths, they are frequently the occasion of great physical suffering, owing to distension by the enlarging gland of its dural encasement: and, furthermore, since they compress the optic tracts and chiasm, they are a usual source of primary optic atrophy.

Largely for palliative reasons, therefore—to check the progressive blindness and to alleviate the headache—operations have been undertaken with the aim of removing the enlarged hypophysis, and several recorded and more unrecorded efforts at extirpation have been made, particularly in London and Vienna, with what has been regarded as a promising measure of success.

However, if we are to profit from the experiences of the earlier operations for goitre undertaken when the physiology of the thyroid and parathyroids was but little understood, it seems premature to undertake operations upon man, at least such operations as have extirpation for their object, before we have some more definite knowledge of the effect upon the body of total hypophysectomy.

Physiologists can attack the problem of the function of a ductless gland in two ways, one to ascertain the effects of injection of the material which it secretes, and the other to study the symptoms which result from its total or partial removal. Although elaborate studies have been made upon the morphology and physiology of the gland, the only striking series of successful extirpations have been those recently recorded by Paulesco,[2] and it has been our aim to test the truth of his assertion, which is contrary to that of many previous investigators, and has been questioned by some later ones[3] that total extirpation of the gland is incompatible with the prolongation of life.

The approach to the sella turcica by experimentalists and by surgeons has been undertaken in a number of different ways. Intracranial routes of access are to be had either by way of the anterior cerebral fossa from in front after elevating the frontal lobes, or by the middle cerebral fossa from the side under the temporal lobe. The extracranial or transphenoidal routes through the nasal, buccal or maxillary cavities, after opening the sphenoidal cells, approach the gland at the base of the skull from below. With the exception of Horsley's unpublished series of cases by the temporal route, all of the successful operations on man thus far recorded have been carried out by the transphenoidal method and seemingly have been only partial extirpations, which may possibly account for their therapeutic success in a number of instances. This has been most striking in the case of acromegaly, operated upon by Hochenegg, the performance being comparable in a measure to a partial thyroidectomy for Graves' disease.

Without entering into a discussion of what will come to be the preferable method of approach to the gland in man, the transphenoidal method for experimental purposes possesses obvious objections, on anatomical grounds, as well as for reasons relating to sepsis. Hence, in our operations, we have been led to accept Paulesco's method, which possesses, at least for experimental canine hypophysectomies, certain unquestioned advantages: for the bilateral cranial opening brings into play the principle of cerebral dislocation of importance in many cerebral operations on man, and this permits of such a degree of elevation of the brain that the hypophysis can be brought clearly into view from the side with but little danger

[1] Read before the American Physiological Society, Baltimore, December 30, 1908.

[2] N. C. Paulesco: Recherches sur la physiologie de l'hypophyse du cerveau. L'hypophysectomie et ses effets. Jour. de Phys. et de Path. générale, 1907, No. 9, p. 441. Also L'hypophyse du cerveau., Paris, 1908.

[3] Gemelli: Biophysikalisches Centralblatt, 1908, III, p. 594.

of injury to the cerebral substance and without risk of compression symptoms.

The procedure which we adopted differs in detail rather than in principle from that of Paulesco, and it has been our aim in this first series of experiments to limit our studies to the effects of total canine hypophysectomy alone, reserving for a subsequent occasion the results of partial extirpations limited to one or another of the anatomical subdivisions of the gland.

The operations have been performed under ether anæsthesia with a preliminary injection of morphia. The animal is placed in the ventral position with a head-rest under the jaws. In order to depress the coronoid process to obtain a direct view of the gland it may be necessary later on to separate the jaws by a gag. The tips of the ears are held together under the throat. The scalp is shaved and prepared and the operative field enclosed with sterile towels with the usual operative precautions. It is well to pin the towels directly into the tissues to prevent their slipping away from the small field of exposure.

A mid-longitudinal incision is made through scalp and aponeurosis from between the superciliary ridges to a point back of the occipital protuberance. After reflecting these superficial coverings the temporal fascia and muscle on each side are divided down to the bone in a line concentric with their attachment and about ½ cm. from the insertion, so as to leave an upper margin sufficient for subsequent reunion. This incision should extend from the orbit back and downward to the posterior end of the zygomatic arch. The muscle on each side is then separated from the cranial vault with a periosteal elevator as low as the zygomatic level and retracted to each side.

We have chosen the left side of the head as the most convenient for exposure of the gland, and consequently the treatment of the two sides of the cranium as well as of the dura differs somewhat in consequence of this. On the side of the approach (left) the zygoma is bared by crowding the tissues forward from its temporal attachment and the arch is resected and excised, as in the usual operative approach to the Gasserian ganglion in man. On the opposite side (right) zygomatic resection is not necessary. Primary openings are then made in the skull with a large trephine, removing a button of bone from the most accessible part—the parietal eminence—of each exposed field. These primary openings are further enlarged with rongeurs, so as to expose a large part of each hemisphere and on the side of proposed approach to the gland (left) the removal of bone is carried well down so as to include the cranial base.

A crescentic incision is then made in the dura on the right side, leaving an opening through which the right hemisphere will be readily dislocated during the necessary subsequent elevation of the left hemisphere in the approach to the gland. The temporal muscle is then loosely replaced over this right hemisphere and the remainder of the operation is carried out entirely on the left side.

Here upon the left we have deviated somewhat from Paulesco's procedure, in making only a small linear opening in the dura as near the basal median line as possible. The opening of the membrane must be made without injury to the overlying brain in order to obviate any obscuration of the field through bleeding from such an accident. Thus the dura under the temporal lobe is gradually elevated, much as in the usual ganglion operation, until the zone of dense attachment of the membrane at the base is reached. The dura just external to this zone is caught up by a small sharp hook and a pin-hole opening made; through this a special cutting hook with a guarded point is inserted, and a linear incision about 1.5 to 2 cm. in length is made across the direction of approach. Through this incision a specially constructed spatula is passed, and the naked temporal lobe, supported by a flattened pledget of cotton, is elevated, giving a ready and free exposure of the pituitary region. A larger incision in the dura is unnecessary and is apt to be the cause of trouble during the subsequent manipulations, in case the cortex should protrude sufficiently through it to cause rupture of the pia-arachnoid with resultant bleeding which quickly obscures the operative field. Furthermore, the preservation of the dura well down beneath the temporal lobe is the greatest source of protection for the cortex during the process of elevation.

Careful swabbing with pledgets of cotton will remove the excess of cerebrospinal fluid, and an excellent view of the pituitary gland just above the third nerve and behind the carotid artery is obtained. The third nerve is an excellent landmark, but the gland itself in any case is easily recognized from its unmistakable reddish color. Occasionally the third nerve is divided and it almost invariably is injured to a degree sufficient to cause a subsequent dilatation of the pupil.

By careful manipulations with delicate blunt-edged spoons it is usually possible, after experience has been gained, to liberate the hypophysis with but slight bleeding, and such extravasation of blood as does occur can almost always be quickly stopped by the temporary insertion of cotton pledgets. In spite of its deep position and vascular attachment, the posterior lobe, possibly owing to its somewhat firmer structure, has been found to be the portion of the gland most easily freed, and occasionally it has been dislocated out of its pocket in the anterior lobe before the entire gland could be removed. We have endeavored, however, to remove the entire gland intact and have succeeded in this endeavor in about half of the twenty cases. In others the gland has been fragmented and has been removed in pieces.

Unless there is some accidental injury to one of the carotid vessels or to the surrounding venous sinuses, the amount of hæmorrhage is surprisingly slight, and after the removal of the gland following the separation of its stalk from the infundibulum it is possible to withdraw from the operative field, leaving it dry and clean and with but little retained blood-clot, as has been evident from the subsequent post-mortem examinations.

The closure of the dura is unnecessary, the temporal

muscles, fascia aponeurosis and skin alone being accurately approximated with fine interrupted sutures. It has been our custom to apply a starched head bandage, to protect the patient from the chance injury of bumping its head while in the ataxic stage of recovery from the anæsthetic. The duration of the operation was usually from two to two and a half hours.

Out of twenty operations five were unsuccessful and, owing either to hæmorrhage which prevented a clean extirpation, or to complications from the ether, these animals died during the operation or were sacrificed before recovery from the anæsthetic. Of the remaining fifteen the majority regained consciousness with the usual promptness and within a few hours were able to get on their feet and walk unsteadily about the room. Within six hours they would drink the water and milk which was sparingly given, and often by the following day they would take solid food, in spite of the recent division of the temporal muscles. Dilatation of the pupil from the third nerve injury was usual on the side of the operation, though this, in a number of cases, passed away by the second day.

Though less active and responsive than after other operations, intracranial or otherwise, nevertheless on the day after the hypophysectomy when at their best they would walk about, eat and drink, and returning to their cages, would rearrange their beds and behave otherwise in a natural way. At this time in the average case the temperature, pulse and respiration would be practically normal. After some hours, however, usually before the second day and occasionally indeed from the time of operation, they would become lethargic, sleeping heavily, paying no attention to comforts of bedding or heaters, and indifferent to the soiling from evacuations. From this condition they would pass into a comatose state with a striking incurvation of the spine, a slow respiration with a long-drawn inspiratory act, a feeble pulse, a perfectly limp musculature and often a subnormal temperature. In one case the rectal temperature before death fell to 25° C. The transition from this deep coma to death was almost imperceptible and unattended by a struggle of any kind. The conjunctival, skin and tendon reflexes were usually retained to the end.

Deviations from this typical course of events occurred in some cases. The lethargic state in some of the animals set in earlier and in a few (four) instances was postponed for four days, once as long as a week. Occasionally, owing we supposed to injury of the pyramidal tract from undue elevation of the temporal lobe (for the fibers of the corona radiata pass, in the canine, quite near the lower surface in their course from the motor cortex to the capsule), the animals showed on the day after operation a rotary progression similar to that seen after unilateral extirpation of the motor field. Fibrillary contractions, trembling and twitching occurred in some instances.

The subcutaneous administration of an infusion of a newly removed canine hypophysis was followed by no appreciable change in the animal's condition on the few occasions when this was carried out.

Postmortem examinations were held on all of the animals without disclosing any adequate cause of death. In a number of instances slight injury of the temporal lobe on the side of approach was observed, but in no case had there been any postoperative extravasation which could have accounted for the fatalities. The sella turcica was found to be completely free from macroscopical evidence of glandular substance. No sections were cut of the tip of the infundibulum, where possibly there may have remained portions of the "pars intermedia" (Hering) which may have accounted for the prolongation of life in the five instances in which the characteristic lethargic state set in later than the first day or two after the hypophysectomy.

In conclusion, we feel that the results of these observations sustain Paulesco's contention that a total hypophysectomy is imcompatible with the continuance of life, although its average duration in our series of typical extirpations has been somewhat longer than that observed in his series of cases. It is a further contention of Paulesco's that the mere separation of the hypophyseal stalk from the infundibulum is equivalent to a total extirpation, and if this is the case it must be a further check upon the attempts at total extirpation, in man, particularly when conducted by the intracranial temporal route, when an accident of this kind is likely to occur.

It is to be inferred from these experimental observations that the surgery of the hypophysis must be limited either to the removal of tumors which may implicate the pituitary gland, or in case of hypertrophy, to a partial hypophysectomy.

EXPERIMENTAL SURGERY OF THE MITRAL VALVE.

By B. M. Bernheim, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

The question having been raised by Sir Lauder Brunton,[1] Can a mitral stenosis be transformed by surgical measures into an insufficiency with benefit to the patient? we have undertaken experimentally to produce and subsequently to relieve such a stenosis. Certain observations with this end in view have already been recorded,[2] and it is my purpose to report further progress, with especial reference to the opera-

[1] Preliminary Note on the Possibility of Treating Mitral Stenosis by Surgical Methods. The Lancet (London), 1902, Vol. I, p. 362.

[2] Cushing and Branch: Experimental and Clinical Notes on Chronic Valvular Lesions in the Dog, etc. Journ. of Med. Research, 1908, Vol. XVII, p. 471.

tive methods which have been used in the attempt to narrow the left auriculo-ventricular orifice; for of all valvular lesions we have found this the most difficult to reproduce.

It may be stated at the outset that though we have been able on numerous occasions to constrict the mitral ring by a suture, and have succeeded in some of these patients in subsequently dividing the constriction, we have not as yet been able to reproduce the typical presystolic murmur or the usual symptoms characterizing the "button-hole" stenosis in man. Hence the question of possible symptomatic benefit from the procedure still remains unanswered, for the lesions that have been made though productive of "murmurs" have merely led to a degree of stenosis to which the heart promptly accommodated itself.

It is necessary to recall that the canine heart, unlike the human, does not lie in contact with the overlying chest wall, and consequently must be approached through the open pleural cavity. Some form of artificial respiration consequently must be employed after the thorax has been opened, and of the two methods which we have used for this purpose—the Brauer positive-pressure apparatus and the simple direct filling of the lungs by means of tracheal canula and bellows—the latter has been found preferable. The tracheotomy is acknowledged to be an objectionable feature and might well be replaced by some form of intubation, but we have never seen any complications follow the immediate closure of the cervical wound after the operation, and other advantages of the method outweigh the uncertainties of the more elaborate positive-pressure apparatus.

Under anæsthesia the trachea is opened between two of the cartilagenous rings by a transverse incision: a large canula is secured after insertion by a tape encircling the trachea, and narcosis is continued by the aid of a Wolff bottle interposed in the tube through which artificial respiration is to be carried on after the chest has been opened.

The approach to the heart has been made as follows: Under the reflected left pectoral muscle about 3½ inches of the exposed fourth or fifth rib with the adjoining costal cartilage is subperiosteally resected. Through the periosteal bed thus left the pleura is incised and the exposed pericardium picked up and divided from apex to base, the edges of the divided membrane being held apart by clamps. If the animal is turned at this time upon its right side the left auricle and ventricle will be uppermost and consequently in the most accessible position for placement of the suture, as will subsequently be described. When the valvular lesion has been made and the heart auscultated, all bleeding having been controlled, the incised pericardium is united, partially or entirely, depending upon conditions, and then, step by step, the pleura, muscular layers, fascia and skin are closed. Artificial respiration, instituted the moment the thoracic cavity was opened, may be discontinued as soon as the chest is again made air tight, and usually spontaneous breathing will be resumed promptly. The wound in the trachea and neck as well as that in the chest is closed without drainage.

The chief difficulties encountered during this long operative procedure are those occasioned by the passage of the cardiac ligature, and, as might be expected, hæmorrhage, either from the wounding of a coronary vessel or from tearing of the cardiac muscle, stands first as the most troublesome and serious. In our early experiments we simply used a single ligature of heavy silk or of linen (Pagenstecher), threaded on a large, round, blunted, curved needle; this was passed and tied so as to gather up a segment of the auriculo-ventricular ring. A particular form of curved needle was devised, having an eye and a fixed handle resembling that of an aneurism needle, and it was found that in this way the tip of the needle could be introduced and made to emerge at the desired points with greater accuracy and security than when a free needle was held in the fingers or in a needle holder. When satisfactorily placed, the ligature was simply tied around the outer wall of the heart with a degree of tension thought to be sufficient to produce the desired lesion. It was soon found that ligation in this way served to cut off the circulation in the superficial vessels covered by the suture with the consequent production oftentimes of an infarct.

To avoid this complication, in a number of cases two separate ligatures were passed through the ring parallel to each other about a centimeter apart: these ligatures were then tied posteriorly and anteriorly in the form of a mattress suture. Complications from this manner of procedure led to further problems. In the first place, unless each ligature was doubled it was found that there was a tendency for it to cut deeply into the muscle at the knots—in fact one suture did actually cut through the thick left ventricular wall within four days. Furthermore, the placing of the double sutures seemed to increase the chances of thrombosis formation, owing to the large amount of foreign material in the cardiac cavity; hence in the more recent and successful experiments we returned to the original method of placing a circular ligature, with the important modification that before tying, the ligature was dipped under the chief coronary vessels, and in this way complications have been completely avoided.

During the course of our studies thirty attempts to produce mitral stenosis have been made; of these thirty animals two or three succumbed promptly of shock or postoperative hæmorrhage before recovering from the anæsthetic; a number of them died from empyema; a few at a later period in consequence of thrombosis formation; ten of them recovered and were allowed to live from a week to three or four months.

It is well known that the pleura of the dog as well as of man is much less resistant to infection than other serous surfaces, notably the peritoneum, and although we observed the strictest aseptic precautions, a number of the animals succumbed within three or four days to infection after an early promise of making a complete recovery. Complications from thrombus formation have been numerous, though less frequent than infection. The heavy linen threads, which were first used for the reason that they seemed to be less liable to cut through the muscle than silk, were given up because in each animal

that lived for any length of time a thrombus was found to have formed around the suture. In one or two that survived only twenty-four hours thrombus formation was found to have already begun. In the hope of avoiding this complication the ligatures were dipped in vaseline before being passed, and on some occasions were coated with surgeon's wax, but the objections to this material have not been entirely overcome by these devices. We have thought that silver wire might possibly be less likely to lead to thrombus formation, but owing to the difficulties of passing it and of preventing hæmorrhage from its points of entry and emergence, as well as from the certainty that, owing to its complete inelasticity, it would cut through the musculature even more promptly than would silk or linen, the idea was abandoned. We have thought that an elastic ligature of some form might possibly be made available, and might possess definite advantages, but we have not as yet attempted to produce stenosis in this way.

One must learn by experience the degree of tension to be put upon the ligature in tying it. We have usually been guided by two signs—the distension of the left auricle, and the cardiac rhythm. The heart usually becomes slowed during the tightening of the ligature, and if it is drawn too tight the beat ceases entirely, becoming first irregular, then with longer and longer intervals between the beats until there is a final cessation. This whole phenomenon is often marked by the independence of auricular and ventricular pulsation.

So far as our experience goes, it matters little whether the ligature be originally placed or tied during systole or diastole —a point formerly thought to be of great importance in suturing cardiac wounds. We have frequently observed, however, that a heart which is beating too rapidly—in other words, one which is "racing"—may often become steadied, slowed, and made to beat more regularly by the passage of the ligature—a phenomenon for which we can offer no explanation. On the other hand, marked irregularity may be caused by the mere resting of the point of an instrument, such as one of pericardial clamps, even lightly against the heart. But the one thing that seems to interfere with the regularity of cardiac action more than any other is the presence of blood in the pericardium; no matter how small the amount it will immediately cause an irregularity and quickening in the beat. This seems to be due to the viscosity of the blood and the mechanical obstruction which it offers to complete diastole. On this account, and also because the blood in clotting offers resistance to the beat, the precaution should be taken, after all hæmorrhage has been controlled, thoroughly to sponge out all blood clots and then gently to flush the pericardial cavity and the outer surface of the heart with warm salt solution. Though we have not practiced it, we have considered the advisability of putting a few drops of a very light sterile oil in the pericardium to act in the capacity of the usual pericardial fluid, thinking that thereby the formation of adhesions might be prevented.

The question of closure of the pericardium has occupied our attention from the start. A certain amount of dilatation of the right ventricle is commonly seen early in these experiments, due probably to the ether and artificial respiration. As the operation proceeds, owing to the manipulations of the heart necessary for the passage of the ligature, this gradually increases and at times may become extreme. Under these circumstances it has seemed unwise to completely reunite the pericardial incision; hence it has been closed in some instances in part only, and in others it has been left entirely open with no untoward results. It is doubtful whether complete closure should ever be made, not only in view of the possible postoperative occurrence of a little bleeding, which, with an open pericardium, would cause little trouble but also on account of this distension of the right ventricle. In fact, this has suggested the idea that it might be of therapeutic benefit to open the pericardium of certain patients who have become bedridden from chronic myocarditis, with the object of relieving the excessive pressure and of allowing more room for the overburdened and dilated heart.

We have frequently been compelled to place one or more sutures in the cardiac wall to control hæmorrhage. On one occasion bleeding from the left auricle, the appendage of which had been picked up by a mouse-toothed forceps and accidentally torn, was easily checked by a mattress suture. Furthermore, in several instances, during the passage of the stenosing ligature a superficial blood-vessel has been wounded, causing severe hæmorrhage and necessitating ligation. In one case, on withdrawing the needle after passing the suture, the mistake was made of not considering its curve, with the result that a jagged tear was made in the anterior cardiac wall. A huge stream of blood was pumped out of the ventricle with every beat, rapidly filling the pericardium and completely obscuring the heart. The wound was controlled by digital pressure until the blood could be sponged out of the pericardium, and three sutures of heavy silk threaded on curved needles passed and tied. In our haste the attempt was made to pass one of these sutures on a straight needle, which was promptly broken in half by the muscular contraction of systole, and the ends had to be left sticking in the cardiac wall until complete closure of the wound was effected, when they were found and extracted. By this time very great dilatation of the right ventricle and auricle had taken place, so that it would have been impossible as well as fatal to close the pericardium. It was therefore left entirely open and the animal lived apparently in perfect health.

As yet, in only one of our cases of experimental stenosis have we successfully operated for its relief, with a perfect recovery; the attempt in a second case was interrupted by a fatal accident in giving the artificial respiration; and one of our most valuable and promising animals was inadvertently used for another purpose some months after the primary operation.

The method of changing the experimental stenosis into an insufficiency needs no especial description. The procedure in general differs from the operation we have described only in the treatment of the heart. For when this has been for the second time exposed by the thoracotomy, MacCallum's cutting

hook (valvulatome) is slipped into the apex of the left ventricle between the arms of an untied mattress suture; the stenosing ligature is cut and the hook withdrawn; then the suture is immediately tied, thus effectually closing the punctured wound of entrance. The treatment of the heart, therefore, is the same as that employed in the production of a primary experimental mitral insufficiency.

This procedure is far easier to carry out than the original stenosing operation; it takes less time; the hæmorrhage is easily and accurately controlled; and the operative mortality is low. This is a point in favor of the future possible operation on man according to Brunton's suggestion, and it is encouraging to think that in the event of such an undertaking, although we shall have to deal with a diseased and overburdened heart, the procedure offers no greater technical difficulties than numbers of others which are in daily practice.

I wish to thank Dr. Emil Goettsch for his assistance in many of these operations.

HYDROCEPHALUS TREATED BY DRAINAGE INTO A VEIN OF THE NECK.

By R. D. McClure, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

The successful treatment of so-called idiopathic hydrocephalus offers a surgical problem, for the solution of which no eminently satisfactory method has as yet been evolved. Though a condition of ventricular hydrops may unquestionably be brought about by a number of different lesions situated at divers places, nevertheless, the essential demand in all cases is to provide for the continuous escape of the obstructed fluid by the establishment of some new channel of outlet.

In the past, many operations have been devised with this end in view. Mere tapping of the ventricles was resorted to at first. This procedure is simple of execution when carried out as is usual through the fontanelle; rather than by the more hazardous approach through the nares, the roof of the orbit or the mouth as some have advocated. Only temporary relief, however, is thus afforded, for in the majority of cases the fluid quickly reaccumulates, often, unfortunately, with a greater degree of tension than before.

The next attempts were directed toward the establishment of permanent drainage. Following the lead of W. W. Keen a number of surgeons have endeavored to accomplish this by making a communication in one way or another between the cavity of the ventricle and the subarachnoid space. Even a successful effort of this kind we now know would not necessarily allow the fluid to escape from the cranial chamber, for in many cases the ventricular cavities and the subarachnoid spaces already communicate, and when this is so the operation at the best merely serves to transfer an internal into an external hydrocephalus, without lessening the amount or tension of the fluid which the cranium holds.

Following the suggestions of Senn, who made use of small tubes inserted through the dura in such a way that they might drain the subarachnoid spaces into the subaponeurotic layer of the scalp, a number of operations upon these lines have been performed at various hands. It has been, however, the unfortunate experience of all who have experimented upon these lines to find that the tubes invariably become occluded with brain tissue, and furthermore that the fluid is not readily taken up by the dense extracranial tissues.

It has been found that in a considerable percentage of hydrocephalic infants it is possible to largely empty the ventricles by lumbar puncture. Thus Cushing [1] records that out of a series of thirty cases of hydrocephalus it was possible in most of them to withdraw fluid from the ventricles by way of the lumbar meninges, showing that the foramina of outlet in the neighborhood of the fourth ventricle may still be patent and yet an obstructive hydrocephalus exist.

On these grounds Quincke, Wynter, and Cushing have each attempted to establish a means of escape for the fluid in the lumbar region. Quincke, after performing a lumbar puncture, blindly inserted a scalpel along the course of the needle into the subdural space, in the hope that the fluid would escape along this pathway into the lumbar tissues. A more open method has been advocated by Wynter, who first performs a laparotomy and then opens the spinal sac from the side in the hope of securing drainage into the lumbar muscles. In those cases in which it was possible to demonstrate the existence of a communication between the ventricles and the subdural space Cushing undertook to establish an outlet for the fluid into the retroperitoneal tissues. In this operation the body of the fifth lumbar vertebra, below the bifurcation of the vessels, is penetrated with a small specially constructed trephine, the anterior half of an interlocking silver canula being inserted in the opening; then, after a median laminectomy and separation of the strands of the cauda equina, the posterior half of the canula is locked in place from behind. The escape of fluid first takes place into the abdominal cavity, but as the freely movable peritoneum easily slips over the abdominal opening of the canula the fluid ultimately escapes into the loose retroperitoneal tissues. The procedure seems particularly applicable to cases in which hydrocephalus accompanies a spina bifida. The operation though delicate and difficult has met with a considerable degree of success.

Krause [2] has more recently attempted to drain directly from

[1] Hydrocephalus. Keen's System of Surgery, 1908, Vol. III, p. 123.

[2] F. Krause: Subkutane Dauerdrainage der Hirnventrikel bei Hydrocephalus. Zentralbl. f. Chir., Aug. 29, 1908, No. 35, p. 61.

the cavity of the ventricle into the subcutaneous tissues of the scalp. A silver tube is inserted through the cortex into the ventricle and is held in place by a flange at its outer end which is secured between the external table of bone and the overlying tissues. In several patients the tube has been left in place for several months. Krause reports a number of cases with favorable results, though none of them have been of very long standing.

Since the completion of our investigations a method has been recorded by Payr[1] in which he likewise makes use of a transplanted blood-vessel. In his operation by the aid of special instruments a vessel is loosely inserted through the cortex into the ventricle, its outer end being sutured into the lateral sinus. An objection to this method would seem to lie in the fact that the inner end of the vessel which extends through a cortex under some degree of compression is floating free in a fluid also under pressure; hence it seems improbable that a vessel which would collapse under such circumstances could readily conduct away the fluid. The anastomosis with an intracranial sinus furthermore would seem to be a most difficult procedure; but should this prove to be feasible it would more nearly approximate Nature's method of draining away the fluid than any method as yet proposed.

The experiments which I have to record were begun a year ago on the suggestion of Dr. Alexis Carrel and, with the encouragement of Dr. Cushing, have been conducted in the Hunterian Laboratory. Our aim has been to establish if possible a permanent drainage between the intracranial subdural space and the cervical venous system, through the interposition of a transplanted blood-vessel.

With the knowledge that in many cases of hydrocephalus fluid from the ventricles finds its way into the subarachnoid (and possibly subdural) space, it would seem that drainage from this space, in these cases at least, would meet the mechanical requirements of the problem. Furthermore, even when the ventricles seemingly do not freely communicate with the subarachnoid spaces it is possible at times, by a proper operation, to transform the internal into an external hydrocephalus. This will be mentioned in the clinical history to be given.

Laboratory Observations.—Six experiments were made upon normal dogs. The vessel selected for transplantation was usually a segment of the external jugular vein taken from the side of the neck contralateral to that of the proposed anastomosis; the femoral was used on two occasions. In the earlier operations, after exposing the skull in the suboccipital region, the bone was trephined and a small circular perforation was made in the center of the exposed dura. One end of the vein was then sutured to the margin of this opening, after which the vessel was carefully drawn through a track made by blunt dissection under the cervical muscles, its lower end being brought out in such a way as to permit of an easy end-to-end anastomosis by the Carrel method with the central end of the newly divided external jugular vein on the same side of the neck.

In selecting a vein for transplantation it is desirable that one be chosen which possesses valves, the vessel being so placed that the valves prevent the upward flow of blood toward the subdural space. In the more recent operations, furthermore, the vein chosen for transplantation was resected so as to include at one end either a point of bifurcation (Fig. 1) or a point where an anastomosing vein of goodly size branched into it. The blade of a fine pair of scissors is then passed

FIG. 1.

FIG. 2.

FIG. 3.

through the two arms of the "Y" and their lumen is opened on the side opposite to the opening into the main vessel. Thus a fairly large rectangular flange which can be trimmed as desired is secured at one end of the main trunk, whose lumen opens in its center (Fig. 2). The segment of vein thus prepared is freely irrigated with salt solution and wrapped in gauze saturated with vaseline while the dura and jugular are being prepared for its reception. The procedure as carried out in our later operations is as follows:

A circular area of the skull is resected just above and posterior to the ear. Within this opening a flap of the exposed dura is turned down and a circular hole about the size

[1] Payr: Drainage der Hirnventrikel mittels frei transplantirten Blutgefässen. Zentralbl. f. Chir., Aug. 29, 1908, No. 35, p. 54.

of the vessel to be transplanted is made in its center. The external jugular vein is then bared by continuing the primary incision over the lower part of the skull and down across the neck, care being taken that it does not directly overlie the the vessel, thus obviating possible complications from scar formation. The exposed jugular is then ligated distally and a small bulldog clamp, protected by rubber tubing, is placed on its central end, after which the vessel is cut across, the ends thoroughly irrigated with warm salt solution, the adventitia trimmed away and the whole smeared with vaseline, as advocated by Carrel.

The vessel to be transplanted is next taken from its protecting gauze and drawn through the hole in the dura from the inside, so that the flanged end of the vessel comes to lie flatly against the inner surface of the membrane (Fig. 3). Several retention sutures are placed at the margin of the flange, anchoring it to the dura, after which a continuous through-and-through suture is carried completely around the periphery. Small blood-vessel needles with a third strand of Chinese silk well saturated with vaseline are used for this purpose. The reflected flap of dura is then replaced and the incision in the membrane is closed with the same materials (Fig. 3). The efficiency of the suturing can be tested by irrigating the subdural space with warm normal salt solution and that of the valves in the vein by irrigating upward through the vessel.

A straight intermuscular channel for the vessel is now carefully made by blunt dissection through the muscles to the exposed end of the jugular vein. The transplanted vessel is drawn through this tunnel and sutured to the central end of the divided jugular by the end-to-end method of Carrel. In no case has there occurred any regurgitation of blood through the vessel beyond its valves on removal of the bulldog clamp. In none of our experiments were there observed any ill effects from the operation. The animals promptly recovered.

After intervals varying from three weeks to three months subsequent to the transplantation the animals were chloroformed and autopsies made. In the first experiment where the vein lay directly under the line of the operative incision, the vessel was much involved in the scar tissue and its lumen was completely obliterated. Adhesions had formed also between the cortex and the dural flap. In the other five cases, where the vessel had been placed away from the line of incision, it was lying rather freely movable, with only slight adhesions. In two instances the lumen was partially obliterated, while in the other three it was patent. Although the vessels seemed smaller than when originally introduced they were elastic and pliable. No histological studies of the tissues have been made.

The results which were obtained in the later observations, in consideration of the fact that the transplanted vessel was practically functionless, were possibly what were to be expected, and it seemed probable that if a copious discharge of fluid from a hydrocephalic head were continuously taking place through the vessel it would in all probability remain patent. As the operation, furthermore, appeared to be free from any particular surgical risk and as it was thought to hold out some promise of benefit, it was believed to be justifiable to employ it in the effort to relieve a case of hydrocephalus which was under Dr. Cushing's care at the Johns Hopkins Hospital and which promised to be a case suitable for this particular measure.

The patient, a ten-months'-old baby, had shown, from the time of its premature birth, evidences of hydrocephalus, and during the three months previous to the final operation had undergone numerous attempts to relieve the pressure symptoms of the rapidly enlarging head. At various hands numerous punctures, ventricular and lumbar, had been made, with only temporary relief. After coming under our observation it was concluded from the results of combined ventricular and lumbar punctures that there was an obstruction in the neighborhood of the fourth ventricle—in other words, that the ventricular fluid communicated but little, if at all, with the arachnoid spaces. In an endeavor to allow vent for the fluid six months before the final operation the bulging lateral wall of the third ventricle had been opened by an operation conducted under the right temporal lobe. For several weeks this measure had promised to give permanent relief, for during this period there was a complete collapse of the fontanelle associated with a rapid improvement in nutrition and a disappearance of the muscular rigidities and other nervous symptoms. This period of temporary improvement was suddenly interrupted by a rapid refilling of the ventricles which in the course of 24 hours led to a tense bulging of the fontanelle which even exceeded the previous condition. The tension became so great that on numerous occasions ventricular punctures were urgently necessitated in order to ward off what seemed to be threatened medullary paralyses from pressure—symptoms accompanied by a slow pulse, convulsions, Cheyne-Stokes' respiration, etc.

One remarkable feature of the case at this time lay in the fact that there was a great difference on the two sides of the head in respect to light transmission. On looking through the head in a saggital direction toward a bright light, the right side of the head—namely, that upon which the operation had been performed—was much more translucent than the left, evidencing, as was supposed, an extracerebral accumulation of fluid on this side—in other words, a unilateral external hydrocephalus; whereas, on the other side the lateral ventricle apparently remained full with a complete distension of the hemisphere as before.

This condition of supposed unilateral external hydrocephalus with fluid in all probability in the subdural space made it seem an unusually favorable opportunity to try and establish an escape for the fluid by the method which had been undertaken in the experiments described above.

The operation was performed July 23, 1908. It proved much more simple in accomplishment than had been the case with the canine experiments. Under cocaine anæsthesia a portion of the cephalic vein was taken from the father's arm,

including the bifurcation of the vessel at the elbow. This vessel was placed in protective vaseline as described in the laboratory experiments. Examination of the child had shown that in the lower portion of the external jugular on the right side there were two valves which prevented any expiratory regurgitation of blood into the external jugular, for the vein proximal to this point dilated markedly when the child cried, and in this part of the vessel could be seen an expiratory pulsation which did not pass above the valves. The condition seemed most favorable therefore for the transplantation, and the presence of these valves in the external jugular did not demand the transplantation of a vessel which also should possess them.

A longitudinal incision was made over the right suboccipital region and carried down in the neck toward the clavicle in the neighborhood of the visible external jugular vein. The soft parts over the suboccipital region were scraped away and an opening about 2.5 cm. in diameter was made in the bone, exposing the dura over the right cerebellar lobe. A flap of dura was turned down with its base toward the neck, and the center of the flap punctured as described above. Through this small opening in the membrane the vein from the father's arm was drawn and the circular flange was sutured in place. The end of the vessel was then passed underneath the splenius and brought out in the lower part of the posterior triangle of the neck, so as to allow a convenient end-to-end anastomosis by the Carrel method with the end of the external jugular just above the situation of the described valves. The wound was then closed without drainage.

The child stood the operation well, and the fontanelle remained soft, but a few hours later a sudden elevation of temperature occurred such as is not uncommonly seen after operations, upon the central nervous system, particularly of infants, supposed in the absence of leucocytosis and with no wound infection to be due to some central thermic disturbance. This unlooked-for complication, which was followed by death shortly after, was the more unexpected since the child had stood the previous rapid withdrawals of fluid by puncture and the earlier much more serious and extensive operation without any complication whatsoever.

The report of these experiments and of this single operative experience with a clinical case is presented merely as a suggestion of what may possibly be accomplished by applying the methods of blood-vessel anastomosis, which have been perfected by Alexis Carrel, to the establishment of drainage in suitable cases of idiopathic hydrocephalus.

AN EFFORT TO DETERMINE THE SENSORY PATH FROM THE OCULAR MUSCLES.

By P. W. Harrison, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

Following the intracranial resection of the *Nervus trigeminus* for neuralgia or—what physiologically amounts to the same thing—the extirpation of the Gasserian ganglion, it has been observed that there is present on the anæsthetic side of the face a very evident loss of the sense of position in many of the muscles supplied by the *N. facialis*. This can be demonstrated in all cases by faradization of the muscles underlying the anæsthetic field, for when thus stimulated, movements in the corner of the mouth, in the ala nasæ or in the orbicularis palpebrarum can be elicited without the patient being aware of them. Though inconspicuous in many patients even though closely observed, in rare instances the condition may be so apparent as to simulate either the flaccidity which accompanies, or the contracture which follows, a slight facial palsy, and certain acts which require a symmetrical movement, such as whistling, are usually performed with difficulty.

This state of things would naturally be expected inasmuch as the muscular branches of the facial nerve contain no afferent fibers, so far as is known, and in the embryo all structures which arise headward from the first visceral cleft appear to receive their sensory innervation from the trigeminus. But according to this view one would suppose that the sensory fibers from the ocular muscles would also be found in the trigeminal nerves, so that by analogy with the condition which occurs in the expressional muscles, some loss of sense of position would be expected in the eye on the side of the neurectomy. This, however, does not occur, for except in the cases, now fortunately rare, in which there has been some slight pressure palsy of the *N. abducens* leading to diplopia from loss of motor function in the external rectus, no disturbance which can possibly be attributed to loss of muscle sense can be detected. This would make it seem probable, on clinical grounds, that there are afferent fibers from the ocular muscles which reach the brain by other pathways than the trigeminal nerves.

The so-called neuro-tendinous spindles which occur in the extrinsic muscles in the eye as well as in other parts of the body have been commonly assumed, since their first discovery, to be organs of muscle sense. The chief reason for regarding them as such seems to be that at present we know of no other organs to which this function may be ascribed and no other function to ascribe to these organs. These "neuro-tendinous spindles," or "neuro-musculo-tendinous end-organs," or "neuro-muscular spindles," as they have been variously called.[1]

[1] As the names indicate, these spindles usually are found in the transition zone between muscle and tendon. Ciaccio, however, in the superior rectus muscle of the human eye found certain

consist of small, transparent, cylindrical structures underlying the sheaths which surround certain tendon fasciculi, near the termination of the muscle fibers, and in each spindle a sensory nerve breaks up into its terminal arborization of non-medullated branches.

These organs were probably observed for the first time in 1875 by Sachs in Kühne's laboratory and independently in 1876 by Rollet. Rollet's studies were chiefly confined to the frog, but the organs were found by Sachs in the tendons also of the salamander, mouse and cat. An accurate description of them was made by Golgi in 1880, who demonstrated their presence not only in the lower vertebrates but in the rabbit, mouse, dog, cat and man; and to him Huber gives the chief credit of recognizing the special nerve end-organ of tendons. Marchi was the first to demonstrate their presence in the tendinous portion of the extrinsic eye muscles of a number of mammals, including man, practically the only tendons of the body in which they had not been observed by Golgi. In this latter situation they have since been made the object of particular study by Ciaccio, Sherrington and Huber.[2]

The distribution of the motor end-plates occupies the central fleshy part of the long ocular muscles, whereas the somewhat smaller medullated fibers regarded as sensory, pass to the tendinous end of the muscles. From their anatomical configuration one would imagine that these myelinate nerve fibers at the insertion end of the muscle must be afferent, for many of them, passing down for a short distance usually on the surface of the tendon as has been described by Sherrington and Huber, then turn back toward the fleshy end of the muscle fibers where their terminal end-organs lie. One finds no motor plates in this situation.

Cattaneo, in 1888, made the first experiments to determine the functions of these spindles which Sachs had believed to subserve the muscle sense. He found no degeneration of the nerves running to these spindles in the extremities after section of the posterior roots of the spinal cord, and likewise none after section of the anterior roots. Following the section of a peripheral nerve, however, degeneration did take place, and Cattaneo concluded from this and from their anatomical position that the spindles in question were sensory nerve endings and probably organs of muscle sense.

In 1897 the question was raised by Sherrington as to whether afferent fibers did not exist in the cerebral nerves controlling movements of the eye—nerves previously regarded as purely motor. This question was answered in a series of papers[3] reporting the results of degeneration experiments. He found after intracranial section of the *N. oculomotorius* in monkeys that all myelinate nerve fibers in the corresponding muscles subsequently degenerated, with the exception of a few fibres, all of small caliber, which supposedly were connected with the ciliary ganglion or sympathetic. They evidently did not come from the *Nn. trigemini*, for after the bilateral intracranial division (in one monkey) of these nerves no obvious impairment in the movements of the eyeballs occurred, nor was there any evident lowering of muscle tonus such as Cattaneo found in the body musculature after section of the posterior spinal roots. Furthermore, no degenerated myelinate fibers were subsequently found in any of the ocular muscles. This widespread degeneration of fibers, presumably sensory in character, which occurred after division of the oculomotor but not after division of the trigeminal nerves, was naturally regarded as an indication of the existence of sensory fibers in the IIIth, IVth and VIth cerebral nerves.

Sherrington further made the experiment of cocainizing the conjunctiva of man and found that no loss of coordinate movement occurs—a further evidence that trigeminal sensation has no influence in the sense of position of the eyes and that an apparatus for muscular sense is required, the only apparent channels for which would seem to be the IIId, IVth and VIth nerves.

Huber and De Witt (1900) in an elaborate study[4] of the end-organs of muscular tissues of many animals (frog, tortoise, bird, rat, cat and dog), using the *intra vitam* methylene blue method, concluded that the sensory nature of the spindles must be regarded as proven by the experiments of Cattaneo and Sherrington, but that anything further as to their special function at present remains uncertain.

Our own experiments were undertaken with the object of observing in the dog degenerations such as Sherrington had found in monkeys after intracranial division of the IIId and Vth nerves. The individual experiments were undertaken as follows:

Under anæsthesia and with the usual aseptic precautions, after reflecting the temporal muscle the cranium was opened on the left side and the desired nerves were divided at the base of the brain—intradurally in the case of the oculomotor and extradurally, as in the usual trigeminal operation in man, in the case of the trigeminus itself. After a period varying from seven to ten days—a length of time which we thought sufficient to allow of complete degeneration of the end-organs—the animals were anæsthetized and either the heart or one of the large vessels was opened and allowed to bleed until the body was exsanguinated. The carotids were then exposed, and a one per cent solution of methylene blue in normal salt solution (according to Ehrlich) was injected, until the scleræ and mucous membranes acquired a distinct blue color. In from thirty minutes to an hour later the bony wall of the orbit was removed and the exposed ocular muscles were resected by

end-organs which were tendinous at both extremities. The Golgi end-organs under discussion are to be distinguished from the Pacini corpuscles, Krause's end-bulbs, etc., of tendons.

[2] G. Carl Huber: Sensory Nerve Terminations in the Tendons of the Extrinsic Eye Muscles of the Cat. Journ. of Compar. Neurol., 1900, Vol. X, p. 152.

[3] C. S. Sherrington: Further Note on the Sensory Nerves of Muscles. Proceedings of the Royal Society of London, 1897, Vol. LXI, p. 247. Further Note on the Sensory Nerves of the Eye Muscles, Ibid., 1898-1899, Vol. LXIV.

[4] G. C. Huber and S. M. De Witt: A Contribution to the Nerve Terminations in Neuro-tendinous End-organs. Journ. of Compar. Neurol., 1900, Vol. X, p. 159.

cutting them as near to their attachments as possible. The appearance of the blue stain in the nerve fibers and endings was then observed under the microscope in the teased-out musculo-tendinous fibers, after which the stained tissues were fixed in ammonium molybdate (Bethe).[1] Treated by this method no degenerated nerve fiber will take up the stain, and any muscle therefore which shows well-stained neuro-tendinous spindles and nerves leading to them could not have had its sensory fibers cut at the previous operation ten days before.

One anatomical difficulty was encountered at the outset. To secure a successful stain it is necessary to remove the muscles from the orbit as quickly as possible, and this, coupled with the fact that the dog has a second row of muscles (retractor oculi muscles) lying within and in close proximity to the four recti, made it difficult oftentimes to accurately identify the individual muscles as they were removed. Fortunately, however, the identification of the inferior oblique was always easy, and a number of our observations depend consequently upon the conditions found in this muscle. It was our expectation, with uniform results in our staining methods, that we could eliminate one muscle after another so that finally it would be possible to determine the sensory pathway from each of them. This plan was frustrated by the fact that even after division of the oculomotor nerve the expected evidences of degeneration were not apparent in the sensory end-organs.

The experiments may be divided into two series. In the first the *N. oculomotorius* was divided by an intradural operation at the base of the brain—a comparatively simple operation in the dog, provided the dura is not opened until the point of attachment of the membrane as it encloses the trigeminal nerve is reached. Then, on elevating the temporal lobe slightly and making a small incision in the dura, through which a smooth elevator can be passed, the glistening IIId nerve comes plainly into view and can be divided with great ease. In all instances the wounds healed without reaction and after a week or ten days the animals were sacrificed and the eye muscles examined in the manner described above. Needless to say, clinical evidence of the division was shown in all cases by the dilatation of the pupil, and a careful postmortem examination was made to assure ourselves of the completeness of the lesions and the absence of local complications. Four observations in this series gave results deserving consideration.

(Number 1.) IIId nerve divided. One rectus muscle showed definite staining of the neuro-tendinous spindles as well as of the sensory nerves leading to them.

(Number 2.) IIId nerve divided. Two superior recti muscles showed good staining of nerves and spindles.

(Number 3.) IIId nerve divided. No nerves or spindles were found to have been stained.

(Number 4.) IIId nerve divided. Three of the muscles, the inferior oblique being one of them, showed a satisfactory stain of nerve and spindles.

The second series of experiments concerned the *N. trigeminus*. The surgical removal of this nerve in the dog presents great difficulties, in consequence of the partial bony encasement of the ganglion. In our earlier experiments we satisfied ourselves with the simple division of the sensory root—an operation which necessitates the careful chipping away of a portion of the tip of the petrous bone. This procedure, unless carried out with great delicacy, will lead to injury of the petrosal sinus and to a degree of bleeding which is incompatible with a successful and certain neurectomy. In order to assure ourselves that the absence of degeneration was not due to our failure to remove the ganglion cells, other operations were performed in which the entire ganglion was removed, in some ways a still more difficult procedure in the dog than simple root division. Six of these experiments were in all respects successful, and the results of these alone need be given.

(Number 5.) Trigeminal root divided. Neuro-tendinous spindles and nerves leading to them successfully stained in the four muscles examined.

(Number 6.) Trigeminal root divided. Nerves and spindles perfectly stained in the inferior oblique muscle.

(Number 7.) Gasserian ganglion extirpation. Nerves and spindles well stained in the five muscles examined.

(Number 8.) Extirpation of ganglion. Fair stain of nerves and spindles in the inferior oblique muscle.

It can be seen from these observations that with the exception of Number 3, in which no nerves or spindles were stained—a result which was attributed to a faulty technique—a satisfactory staining of these supposedly sensory endings was present in certain of the muscles supplied by the oculomotor nerve at a sufficient time after its division to allow, as we supposed, for complete degeneration in case this were to occur after the neurectomy.

Though the possibility that the IVth and VIth nerves might constitute the sensory pathway in question seemed remote, it was our intention to undertake a third series of experiments in which the IIId, IVth, Vth and VIth nerves should all be cut, but we were unable to overcome the surgical difficulties of this procedure in the time at our disposal. The only animal upon which the operation was successfully carried out succumbed to an infection after a lapse of three days—a period not sufficient for the purposes of the experiment.

A further series of observations should be made, with division of the post-axial fibers of the sympathetic, to eliminate this nerve from the problem, though it is improbable that section of the sympathetic would lead to any evidences of degeneration in these organs under discussion.

The results of our experiments thus briefly recorded do not coincide with those obtained by Sherrington, and furthermore are opposed to our own preconceived views of the matter acquired from the clinical observations mentioned in the intro-

[1] This, briefly, is the technique which Prof. G. Carl Huber has himself carefully described, and one of us (Harrison) was privileged to learn it at first hand in his laboratory. We are further indebted to Prof. Huber for his kindness in looking over some of the specimens obtained from our own experiments.

ductory paragraphs. Whether our failure to find evidence of degeneration in these organs after dividing the oculomotor nerve is due to the fact that the pathway from the neuro-muscular spindles lies elsewhere than in these nerves; or, that through some technical fault we were unable to get the expected evidence of degeneration; or, that these, after all, are not organs of muscle sense but serve some entirely different function, must be left undetermined for the present.

Our failure to confirm the results of previous investigators along these lines we trust will stimulate others, as it will ourselves, to further investigations, for it is a matter of considerable physiological interest and importance to know whether the oculomotor nerves are actually mixed nerves or contain, as was long supposed, purely efferent fibers. The absence of any loss of muscle balance following division of the trigeminus, as well as the failure to find any degenerations in what are supposed to be the musculo-sensory organs of the ocular muscles, confirms Sherrington's observation that the trigeminal nerves at least do not convey the sensory impulses from the muscles in question.

A NOTE ON SOME METHODS OF ANASTOMOSING BLOOD-VESSELS.

By B. M. Bernheim, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

Cuff Method of Anastomosis.

The careful removal of the adventitia from the divided ends of the blood-vessels is one of the most important steps in making a successful anastomosis. This is easily accomplished in the case of the artery, but, owing to the great contractility of the vein, considerable time and undesirable handling is often required, resulting not infrequently in injury to the intima with subsequent thrombus formation.

To avoid this the following method is suggested of everting a cuff of the vein (or artery if desired), whereby the removal

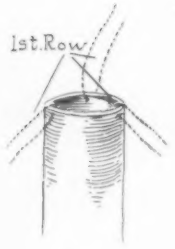


Fig. 1.

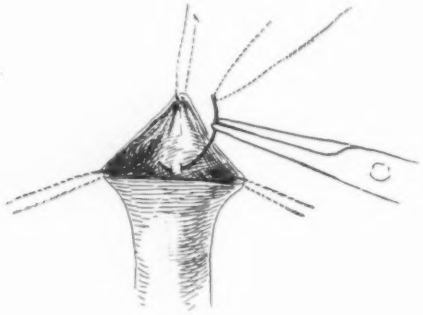


Fig. 2.

of the adventitia is rendered unnecessary and in the suture intima is of necessity apposed to intima.

After dividing the vein or on removing a section of it, without further handling, three stay sutures are applied at equidistant points around the lumen just on the cut edge, according to the method of Carrel (Fig. 1). By equal traction upon these sutures the mouth of the vessel will be thrown open into a wide triangle (Fig. 2). With a small curved French needle, threaded with the finest silk, three additional stay sutures are placed in the same lines as the former ones, but about one-fourth of an inch or more down *in* the lumen of the vessel (Fig. 3). Traction on the second row in one direction and on the first row in the opposite direction will evert the cuff (Fig. 4). The anastomoses can then be accomplished by Carrel's method, the needles and threads of the second three stay sutures being used for catching up and triangulating the end of the artery at three corresponding points[1] (Fig. 5).

At the completion of the suture the cuff (1) can be thrown forward and sutured to the adventitia of the artery (Fig. 6); or (2) can be turned back and sutured to the adventitia of

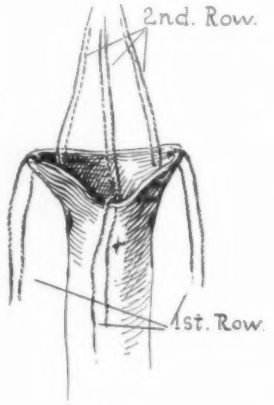


Fig. 3.

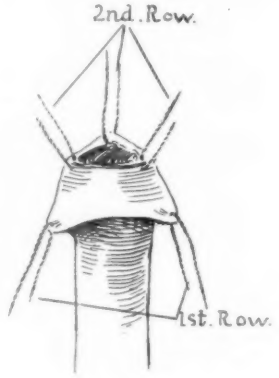


Fig. 4.

the vein; or (3) in case a segment of vein is to be interposed in an arterial defect, the two cuffs can be made of such size that, when thrown back from each end of the vessel, they will meet and can be sutured together, thus making a vein of double thickness.

Doubling the Vein.

To restore a defect in an artery, such as occurs after the extirpation of an aneurism, either a segment of another artery or of a vein must be used. As there are no superfluous

[1] Conditions might arise where it would be desirable to have a very large cuff. This could easily be made by everting the vessel over the end of a canula, similar to but with a longer cylinder than that devised by Crile for transfusions.

arteries in the body and their preservation for purposes of transplantation has not as yet been rendered practicable, it is necessary to use a vein.

Owing, however, to their relative structural weakness, veins

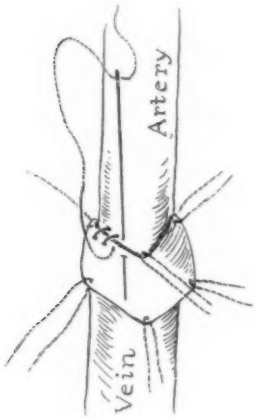


Fig. 5.

Fig. 6.

are not well adapted to endure arterial pressure, and consequently after a transplantation a considerable, often an astonishing, dilatation occurs; this is followed by an hypertrophy of the venous walls, which may in course of time increase to such an extent as to obliterate the lumen, for an early sclerosis is not an infrequent occurrence.

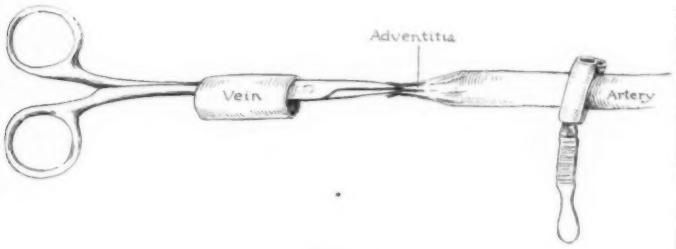


Fig. 7.

In order to lessen this strain and also to render more secure the lines of suture, the following method of doubling or even tripling the thickness of the transplanted veins is suggested.

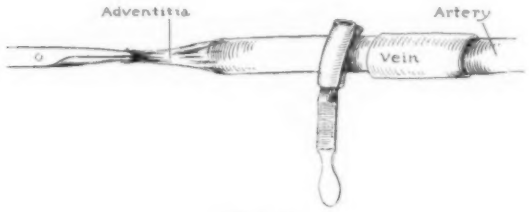


Fig. 8.

Two segments of vein are taken—one almost twice as long as the other. The longer piece is threaded on a "mosquito" clamp, which then grasps the adventitia of one end of the artery (Fig. 7), thus allowing the vein to be threaded over the artery to a point beyond the bulldog clamp obstructing the blood-flow (Fig. 8). The shorter piece of vein is then anastomosed between the two ends of the artery. After removing the bulldog clamps and controlling all leakage from the two lines of suture the longer piece of vein is slipped over the anastomosed segment, in which position its ends are attached to the adventitia of the artery by three interrupted sutures (Fig. 9).

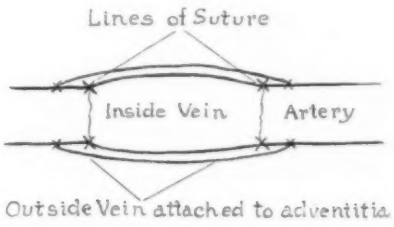
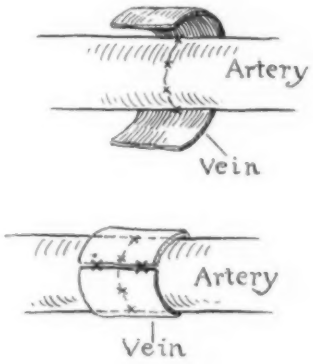


Fig. 9.

Securing the Line of Suture.

Just as in intestinal work, so in blood-vessel sutures conditions arise where it might be advisable to protect and strengthen the line of suture. This can be done either by "threading" a piece of vein over the line of suture, as described above, or by first performing the anastomosis and



Figs. 10 and 11.

then folding around the suture a segment of vein previously slit open (Figs. 10 and 11).

A number of anastomoses have been performed by these methods, full reports of which, with the microscopical findings, it is purposed to give in a later paper.

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ON THE EFFECT OF NARCOSIS UPON THE BODY TEMPERATURE.

By S. Griffith Davis, M. D.

(From the Hunterian Laboratory of Experimental Medicine.)

In his important monograph published in 1880, Otto Kappeler[1] laid stress upon the loss of body temperature of human patients during anæsthesia. In twenty surgical etherizations he found an average fall of 0.68° C., a maximum loss of 1.5° C. and a minimum loss of 0.3° C. Excluding the cases with preexisting fever, there was an average loss of 0.52° C. The fall of temperature becomes first apparent in from ten to twenty minutes after beginning inhalation. The shortest time in which the greatest fall was observed was twenty minutes; the longest time was two hours. The average greatest fall occurred in 60.4 minutes. Occasionally a slight temporary rise was observed coincident with the struggling of the primary stage of anæsthesia.

Kappeler also made observations on thirty human patients under chloroform and found with this drug an average loss of temperature of 0.59° C., the extremes varying between 1.1° C. and 0.2° C. Usually at the cessation of anæsthesia the temperature was found to return slowly to the normal, though in a few instances it continued to fall. In non-febrile cases the average loss was 0.53° C., corresponding practically with that observed under ether. The first drop never appeared earlier than ten minutes after beginning the inhalation, the average time being from fifteen to twenty minutes. The lowest fall occurred at a time averaging fifty minutes when the most profound appearances of narcosis were for the most part over, though it may be said that the more profound the narcosis the greater was the fall in temperature. According to Kappeler's observations it was rare for the temperature to return to the normal in less than an hour; occasionally it required five hours. During the period of active excitation in a few instances a slight primary elevation of circulation and temperature was noted.

Similar observations were published in 1888 by H. A. Hare,[2] who found in thirteen cases an average loss of 2.5° F., the greatest loss observed being 4.4° F. and the least 1.2° F. The temperature in these cases was taken by axilla. In thirteen instances in which the duration of anæsthesia as well as the character of the operation was noted, he observed an average fall of 2.32° F. The maximum loss occurred in a case of carcinoma of the breast, namely, 3.15° F.; the minimum loss, namely 0.8° F., occurred during a thoracotomy for empyema. Hare also found that the rectal temperature of a dog, during the course of an hour's etherization might fall from 8° to 10° F. below the normal.

Dastre's comprehensive work on anæsthesia (1890)[3] speaks briefly of Kappeler's observations and regards the diminution of oxidation as the principal cause of the lowered temperature rather than immobility or radiation of heat from the uncovered portion of the body. The studies of Paul Bert and of Rumpf favor this view. In addition to this action of the drug on the tissues, Dastre considers that the thermoregulatory centers are probably affected as well.

One of the most comprehensive reports on this subject, based upon the results both of experimental and clinical observations, was made by Dudley P. Allen[4] in 1897. Thirty-five experiments were made upon dogs showing that they lose heat in a marked degree under prolonged anæsthesia with the body exposed to ordinary room temperature, e. g. 65° to 75° F.; also that this loss may be partially if not entirely obviated by preventing the radiation of heat with abundant coverings. He found further that the temperature may actually be increased if in addition to these coverings the animal be surrounded with hot water bottles. It seemed obvious from these observations that the alterations in temperature were attributable to the anæsthesia, and it was noted that the temperature after cessation of the anæsthetic tended to return to the normal, whether it had been forced above its proper level by external heat or had fallen below in consequence of exposure. This return was more rapid in the case of ether than of chloroform. He found, too, that in a room having an unusually high temperature, namely, from 93° to 96° F., the body temperature of the animal was rapidly raised under anæsthesia, in some cases even to 4.6° F., irrespective of the degree of exposure of the body. In the human patient he found that a loss of from 0.2° F. to 2° F. commonly occurred, 0.6° F. representing the average loss in the eighty recorded cases.

In 1903 W. H. Morley,[5] in an article devoted to this same matter, also describes the lowering of body temperature under ether anæsthesia. He favors the view that the lowered temperature is due to increased output of heat in consequence of dilatation of the cutaneous vessels and to lessened heat production from diminished muscular movement. He urged that stringent precautions be taken against the loss of body heat during anæsthesia by having the patient well protected and in a warm operating room, believing that many of the so-called postoperative pneumonias are a consequence of the patient being chilled while in a state of narcosis.

In his well-known volume, W. F. Hewett[6] comments upon the surgical importance of maintaining the body heat, in view of the loss of temperature which invariably occurs during the

[1] Kappeler: Anæsthetica. Deutsche Chirurgie, 1880, pp. 33 and 168.

[2] Hare: Experiments to Determine the Influence of Etherization on the Normal Bodily Temperature, etc. Therapeutic Gazette, 1888, Vol. XII, p. 317.

[3] A. Dastre. Les anesthésiques: physiologie et applications chirurgicales. Paris, 1890.

[4] Allen: Effect of Anæsthesia upon the Temperature and Blood-pressure. Tr. Am. Surg. Ass., 1896, Vol. XIV, pp. 367-389.

[5] Morley: The Effect of Anæsthesia upon the Body Temperature. American Gynecology, 1903, No. 3, pp. 300-304.

[6] Hewett: Anæsthetics and Their Administration, 3d Edition, 1907, p. 234.

administration of ether and chloroform. He mentions further that "covering cutaneous areas with towels wrung out of antiseptic solutions is open to considerable objection."

These and similar reports have thus evidenced the possible relation between postoperative pulmonary complications and the lowering of temperature due to the combination of anæsthesia and exposure. A number of particularly cautious operators consequently have made it a rule to protect the body against such a possible thermic loss by insisting upon the employment of some form of heated operating table, such

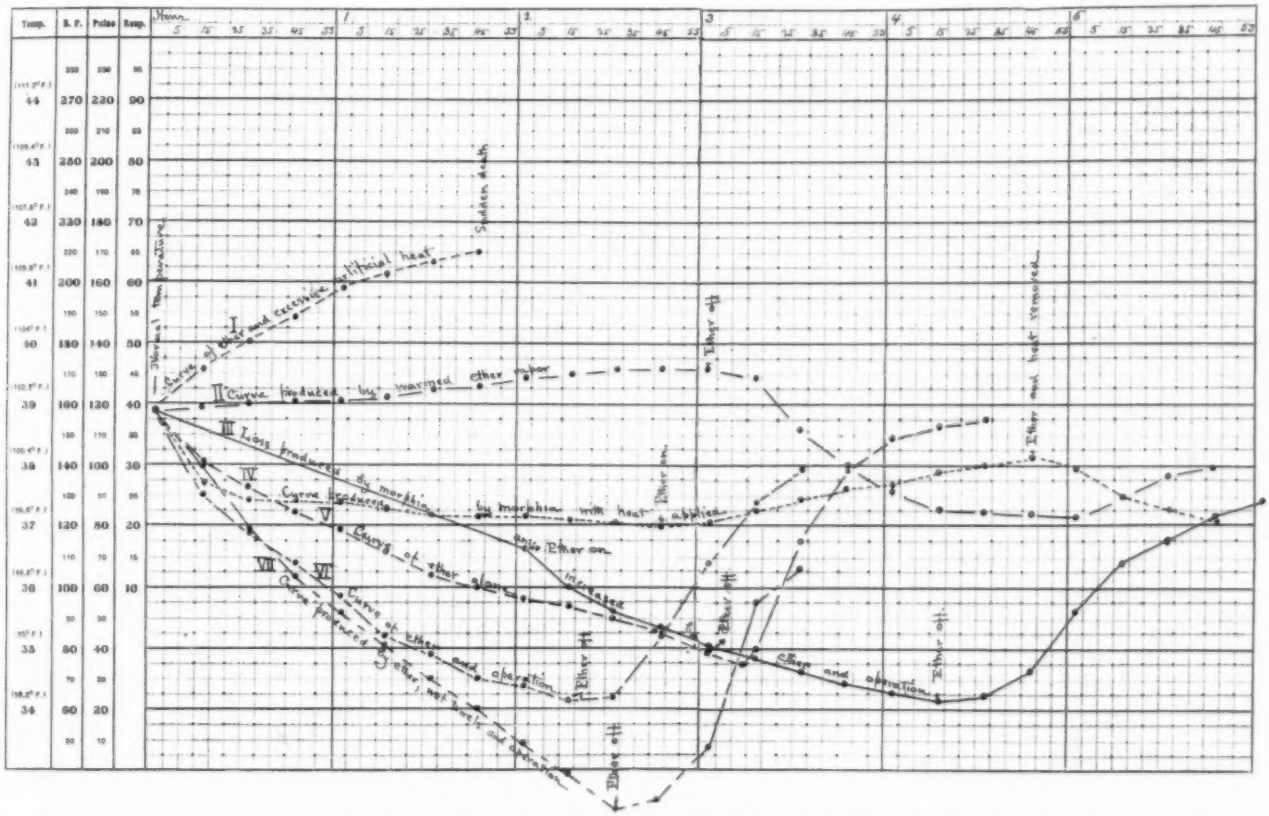

Chart 1.—A composite of the curves of all the observations under seven different conditions. (1) Curve produced by ether and artificial heat, raising the temperature to such a degree that death resulted. (2) Showing practically normal level under warm ether vapor alone, and support of body temperature by this means with fall in temperature after cessation of anæsthesia. (3) The average curve produced by preliminary morphia increased by operation under ether. (4) Curve produced by morphia with application of external heat. (5) Curve produced by ether alone without operation. (6) Curve as influenced by ether and operation together. (7) Curve produced by ether and operation, showing increase in thermic loss when the patient's body is wet.

as that of Kronig, but it must be acknowledged that the importance of these matters has been overlooked or ignored by the greater number of surgeons.

From the Hunterian Laboratory a year ago, C. W. Mills[7] made a report upon the alterations of body temperature occurring in anæsthetized animals, and it is the purpose of this paper to record further observations made along similar lines, and to suggest applications which may be of some practical importance. For greater accuracy in the work special charts were designed for the recording of temperature alongside of the blood pressure, pulse and respiration, so that the plotted curves become comparable in a measure to the kymographic tracings of the physiological laboratory. The keeping of such a record adds considerably to the anæsthetist's duties, but by a method of continuous auscultation, the cardiac and the respiratory sounds can be transmitted directly to the ear and thus easily recorded, without the necessity of feeling for the pulse.[8] The temperature records were taken per rectum and accurate centigrade clinical thermometers were used, which

[7] Mills: On the Alterations in Body Temperature Produced in Dogs by Morphia and Ether. Johns Hopkins Hosp. Bull., 1907, Vol. XVIII, p. 469.

[8] This simple device and some of its advantages, both to the operator and the anæsthetist, have been described by Dr. Cushing (J. Am. Med. Ass., 1909, LII, p. 187).

The apparatus consists of the transmitter of a Bowles stethoscope connected by a rubber tube 36 inches long with a hard rubber ear-receiver of a phenendoscope. A metal headband, such as is used by a telephone operator, holds the ear-piece against the external auditory meatus. The bell of the stethescope is strapped on the patient's chest with adhesive plaster over the point of maximum impulse.

With this method of continuous auscultation, not only can a

not only allowed a lower registration than the simple clinical instruments which had been employed by Dr. Mills, but also a continuous reading.

For the sake of uniformity, the laboratory observations were made almost exclusively upon short-haired dogs of the fox-terrier type.

Experimental Observations.

(I) *The effect of confinement alone in the usual dorsal position on the table.*

No. 1. Weight 5 kg. After confinement on the table for two hours, a fall of 0.5° C. occurred in the latter part of the observation.

No. 2. Weight 6 kg. No variation in temperature occurred in this animal, although he remained on the table for two hours.

(II) *The effect of morphia alone with the animal in the same position.*

No. 3. Weight 9 kg. Morphia 16 mg. Temperature of room 19.3° C. Temperature of animal before morphia was given 38.6° C. One-quarter of an hour after morphia it had fallen to 38° C.; in half an hour to 37.6° C.; in three-quarters of an hour 37.4° C.; in one hour to 37.3° C.; in two hours to 37.2° C.; making a total loss of 1.4° C. (2.52° F.) in two hours, most of which had occurred during the first hour.

No. 4. Weight 12 kg. Morpnia 16 mg. Temperature of room 22.2° C. Temperature of animal before morphia was given 39° C. During the first fifteen minutes the animal was very restless, and the temperature remained stationary; during the next fifteen minutes there was a fall to 38.5° C.; in half an hour it had fallen to 38° C.; in three-quarters of an hour to 37.6° C.; in one hour to 37.5° C.; in one hour and a quarter to 37.4° C., where it remained for two and a half hours. At this time the confining

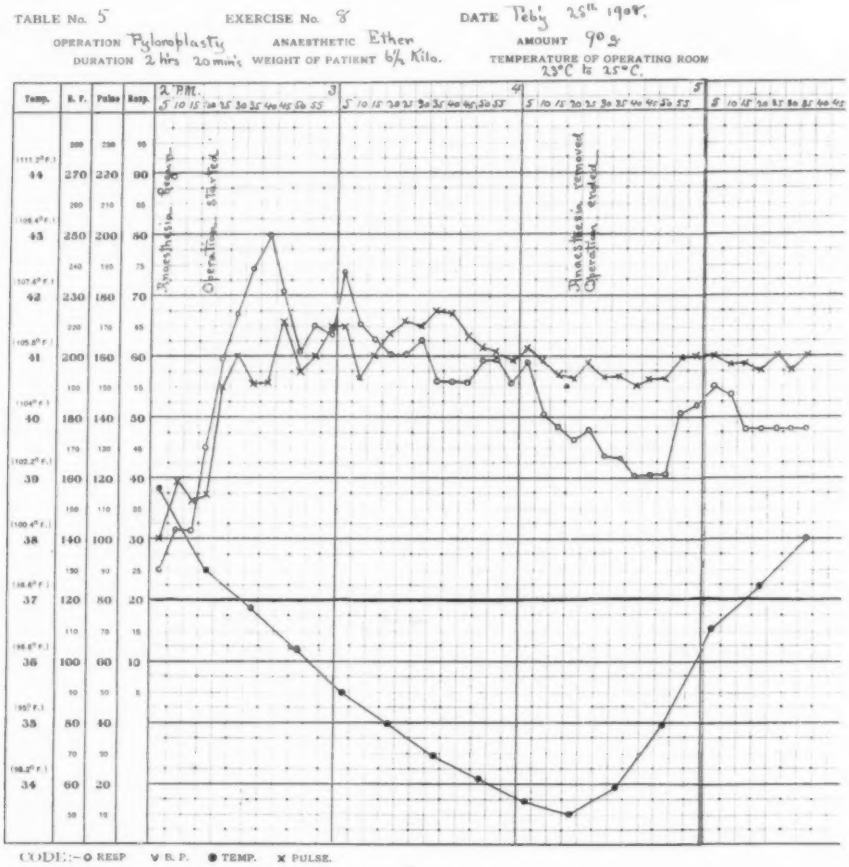

Chart 2.—Individual chart showing alterations of pulse rate, respiration and temperature during the course of an operation for pyloroplasty in a dog under ether anæsthesia without preliminary administration of morphia; ordinary operating room conditions without special precautions to preserve body temperature by external application of heat. Note rapid fall of temperature of over 9° F. from the first administration of the anæsthetic until its removal, with prompt return to the normal after cessation of administration.

Two docile animals were placed in the usual dorsal position, where they were confined and remained exposed without covering. Though kept reasonably quiet by cajoling and patting, some restlessness was inevitable and may have served to keep up the body temperature.

record of pulse and respiratory rate be easily kept during the operation, but the anæsthetist is able to continuously estimate their activity without the necessity of disengaging a hand for the palpation of a peripheral vessel or of looking away from his immediate task to observe respiratory movements.

straps were loosened and more liberty was given. The temperature immediately began to rise, reaching 38.2° C. at the end of two hours. The animal was then freed and allowed to run about. The temperature immediately made a rapid rise, reaching 39° C. in three-quarters of an hour. During the first hour the fall had been very rapid, amounting to 1.4° C.; in the second hour it only amounted to 0.1° C., making the total fall of 1.5° C. (2.7° F.) in two hours. The pulse and respiration of these animals fell rapidly during the first hour and then remained about stationary.

(III) *The effect of ether alone with the animal in the same position* (cf. Curve IV, Chart 1).

of 0.7° C. occurred. The temperature of the room at the conclusion of the observation was 20° C.

(IV) *The effect upon temperature by an operation under ether alone* (cf. Curve VI, Chart 1 and Chart 2).

Observations were made upon seven animals employed in the operative surgery course. Their weight varied from 5 to 7.4 kg. The temperature of the room varied from 20° to 25° C. The average body temperature before anæsthesia was 38.8° C., and the average fall after two and one-quarter hours reached 34.1° C., making a total loss of temperature of 4.66° C. (8.39° F.). The

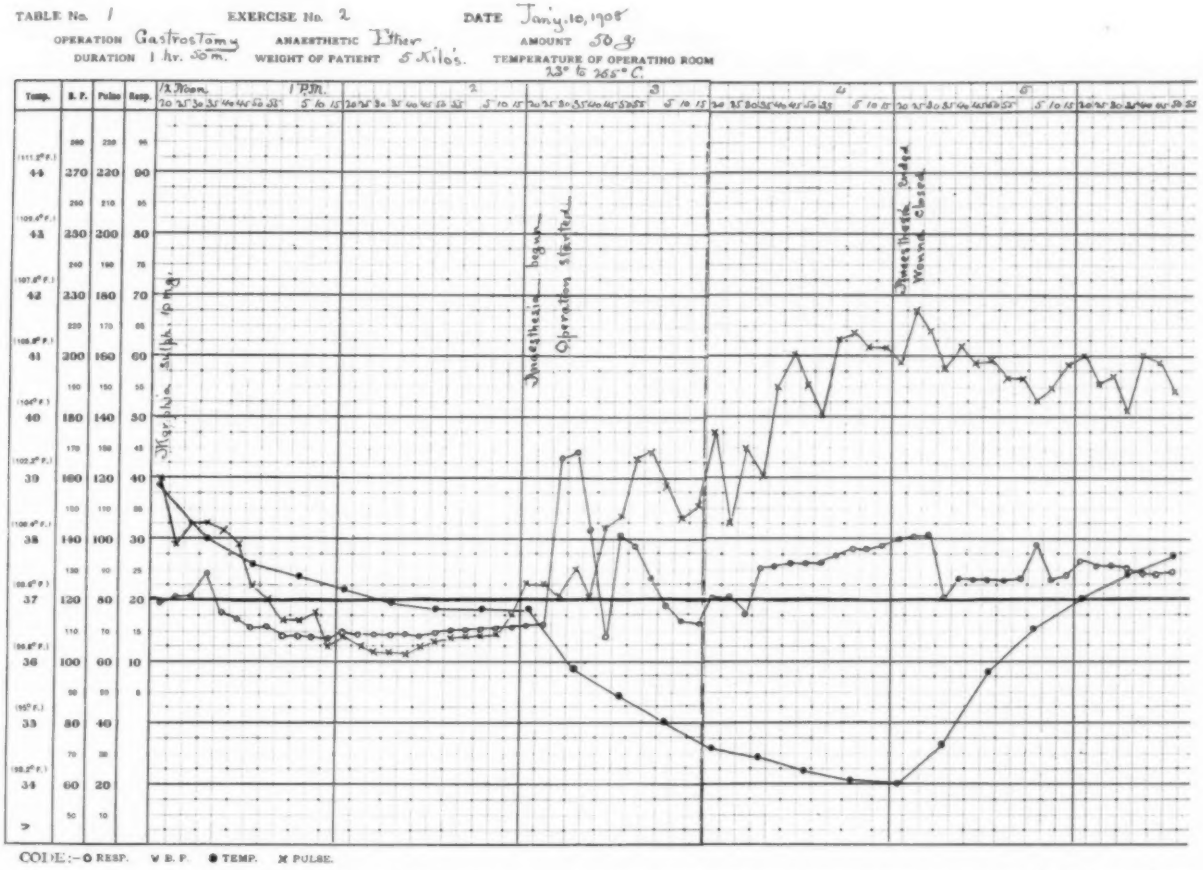

CHART 3.—Individual chart showing the curve of respiration, pulse rate and temperature as affected by a laparotomy on a dog under ether anæsthesia after preliminary administration of morphia. Note the fall in rate of pulse and respiration and the drop in temperature under morphia alone, and the immediate increase in the latter after administration of anæsthesia.

No. 5. Weight 6.5 kg. Temperature of room 25.5° C. The body temperature was 39° C. before the administration of ether and remained stationary for five minutes, when it commenced to fall rapidly. In fifteen minutes it had fallen to 38.2° C.; in half an hour to 37.6° C.; in three-quarters of an hour to 37.2° C.; in one hour to 36.9° C.; in one hour and a quarter to 36.6° C.; in one hour and a half to 36.2° C.; in one hour and three-quarters to 36° C.; in two hours to 35.8° C., and in three hours to 34.9° C.; making a total fall of 4.1° C. (7.4° F.). Fifteen minutes after ether was discontinued the temperature returned to 35° C.; in the next fifteen minutes there was a rapid rise to 36.8° C., and in the following fifteen minutes to 38° C., making a total rise of 3° in half an hour. Then for three-quarters of an hour a gradual rise

figures for the individual cases, with the average fall in fifteen minutes, are given in the following table:

	Before ether.	15 minutes later.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 6....	38.7	37.5	36.8	36.1	35.6	35.2	34.8	34.2	?	....
No. 7....	39	38	37.5	36.8	36.4	35.8	35.5	35.1	35	34.7
No. 8....	38.8	37.1	36.7	36.5	35.8	34.5	34.4	34.2	34	....
No. 9....	38.2	36.8	36.1	35.8	35.5	34.6	34.4	34.1	34	33.6
No. 10....	38.6	36.5	36.2	35.5	35	34.5	34.2	33.9	33.3	33
No. 11....	39	37.4	36.9	36.5	35.5	34.9	34.4	34	33.8	33.5
No. 12....	39	38.5	37.8	37.1	36.7	36.5	36.3	35.9	35.8	35.7
Average.	38.8	37.4	36.8	36.3	35.8	35.1	34.8	34.5	34.3	34.1

(V) *The effect of ether and operation upon the temperature curve after preliminary morphia* (cf. Curve III, Chart 1 and Chart 2).

Observations were made upon twenty-five animals, weighing from 5.5 to 9 kg. The temperature of the room varied from 20° to 25° C. The body temperature in ten instances was taken immediately before the 16 mg. of morphia was given. The average was found to be 38.9° C. (102° F.). Two hours later the temperature had fallen to 36.6° C., making a total fall of 2.3° C. (1.14° F.) in two hours due to morphia alone. The greater fall under morphia before ether was administered in the temperature of the animals of this group over those of Group II is probably due to the fact that they were in colder surroundings.

A subsequent administration of ether with the preparations for and performance of an operation led to a further drop, as shown in the following table, making a total average fall of 4.81° C. (8.65° F.) in four hours, from the combined effect of morphia, ether and the operation.

	Before morphia.	2 hours later when ether was started.	15 minutes.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 13....	38.8	37.2	37	36.8	36.5	36.2	35.8	35.6	34.8	34.6	....
No. 14....	39.2	36.5	36.3	36.2	35.7	35.2	?	....	....	....	....
No. 15....	....	36.8	36	35.3	35.2	35	?	....	....	....	....
No. 16....	...	37.3	36.8	36.2	36	35.8	35.2	35.2	?	...	....
No. 17....	39	35	34.7	34.4	34.2	33.8	33.3	33.1	32.8	32.3	32.3
No. 18....	39	36.8	36.5	36.3	35.9	35.7	35.6	35.4	35.3	35.3	....
No. 19....	38.6	36.4	35.8	35.6	35.4	35.2	34.7	34.3	34.2	34.2	....
No. 20....	..	37.7	37.2	36.4	35.2	35.1	34.8	34.7	....	....	....
No. 21....	....	37.2	36.1	35.6	35.1	34.3	33.8	33.4	33.2	....	....
No. 22 ...	....	37.6	36.6	36	35.4	35.1	34.8	34.4	34.2	33.8	33.3
No. 23....	38.7	36.2	35.4	35.2	35	34.8	34.5	34.3	34.1	34	...
No. 24....	39.2	36.7	36	35.2	35	34.5	....	....	33	....	....
No. 25....	39.4	34.8	34.8	34.8	34.7	34.6	34.6	34.5	34.5	34.4	34.2
No. 26....	....	36.5	35.8	34.9	?	....	....	....	....	....	....
No. 27....	....	37.6	36.7	36.0	35.1	?	....	....	....	....	....
No. 28....	....	36.8	36.5	36.1	36	35.8	35.7	35.6	35.5	35.5	35.1
No. 29....	38.6	36.8	36.4	36.4	36.2	36.1	36	35.8	35.6	35.6	35.6
No. 30....	....	37	36.4	36	35.5	35.4	35.1	34.8	?	....	....
No. 31....	....	36.8	35.8	35.4	35	34.6	34.4	34.2	34.1	34	...
No. 32....	....	35.9	35.5	35.2	34.9	34.8	34.7	?	....	....	....
No. 33 ...	....	35.8	35.3	35.1	34.7	34.8	34.7	?	....	....	....
No. 34....	....	36.2	35.9	35.4	34.9	34.4	?	....	....	....	....
No. 35....	....	37.2	36.6	36.2	35.7	35.5	35.2	34.9	34.6	34.4	?
No. 36....	....	36.3	35.8	35.3	35	34.8	34.5	?	....	....	....
No. 37....	38.8	36.6	35.4	34.8	34	33.7	33.4	33.2	33.1	33	....
Average.	38.9	36.6	36	35.6	35.2	35	34.8	34.6	34.2	34.2	34.1

(VI) *The effect of chloroform and operation upon the temperature curve after preliminary morphia.*

Observations made upon three animals: Weight not recorded. The average temperature of two of them before morphia was given was 38.8° C.; the subsequent individual and average fall is given in the following table:

	Before morphia.	2 hours later when chloroform was started.	15 minutes.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	2 hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 38.....	38.9	36.7	36.9	36.5	36	35.6	35.4	35	34.7
No. 39.....	38.8	36.6	35.9	34.4	34.1	?	...	....	....
No. 40.....	....	35.8	35.5	35.3	35	35	34.7	?	....
Average.....	38.8	36.4	36.1	35.4	35	35.3	35.2	35	34.7

(VII) *The effect of surrounding the field of operation with wet towels upon the temperature curve produced by ether and operation.*

In two abdominal operations under ether with the field of operation surrounded with wet bichloride towels, the temperature dropped from 39° C. to 32° C., making a total loss of 7° C. (12.6° F.) in two and three-quarter hours. The average fall is noted in detail in the following table:

	Before ether.	15 minutes after ether was started.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.	2¼ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 41....	38.6	37.5	36.7	35.8	35	34.4	33.8	33.2	32.4	31.9	31.3
No. 42 ...	39.5	38.8	37	36.7	36.4	36.1	35.1	34.8	34	33.5	33.2
Average.	39	38.1	36.8	36.2	35.7	35.2	34.5	34	33.2	32.7	32.2

(VIII) *The effect of surrounding the field of operation with wet towels upon the temperature curve produced by morphia, ether and operation.*

In two abdominal operations in which 16 mg. of morphia had been given to the animals two hours before the administration of ether and the field of operation surrounded with wet bichloride towels, the temperature fell from 38.6° C. to 32° C., making a total loss of 6.6° C. (11.9° F.) in four and a quarter hours (two hours under morphia and two and a quarter hours under ether). The average fall is shown in the following table:

	Before morphia.	2 hours later when ether was started.	15 minutes.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 43....	38.8	35.3	34	33.3	32.8	32.5	32.2	31.3	31	31	....
No. 44....	38.5	36.9	36.4	35.9	35.4	35.1	34.9	34.5	33.9	33.2	32.3
Average.	38.6	36.1	35.2	34.6	34.1	33.5	33.5	32.9	32.4	32	....

(IX) *The effect of the external application of heat upon the temperature curve produced by morphia alone.*

No. 45. Weight 5.4 kg; body temperature 38.3° C. Sixteen mg. of morphia were given and the animal allowed to remain in a cool room for fifteen minutes. During this time the body temperature fell to 37.6° C. The animal was then transferred to a room varying in temperature from 20° C. to 22.8° C., and confined in the dorsal position well protected with artificial heat applied externally. The temperature of the electric thermopyle was raised until a thermometer put under the animal's back registered from 50° to 52° C. The body temperature remained about stationary, with a slight inclination upward or downward, according to whether there was more or less heat applied. In two hours the artificial heat and coverings were removed. The temperature immediately began to fall, though the temperature of the room had meanwhile been increased to 22.8° C., and it continued to fall for one and a half hours until there was a loss of 0.8° C. It then remained stationary for half an hour. The animal was then released and the temperature slowly rose 0.7° C. in the next hour.

No. 46. Weight 7.4 kg.; body temperature was 38.5° C. After 16 mg. of morphia the animal was allowed to remain in a cool room for half an hour, the temperature falling meanwhile to 37.5° C. He was then transferred to a warm room, with a temperature of 22° C., where artificial heat was applied. The temperature made a gradual rise of 0.3° C. in 45 minutes. At this time the external heat was lessened and there was a corresponding fall of 0.3° C. during the following hour.

No. 47. Weight 6 kg.; body temperature 38.6° C. After 16 mg. of morphia in cold quarters a loss of temperature of 0.6° C. occurred in 15 minutes. The animal was then transferred to a warm room varying in temperature from 18° to 21° C. and con-

fined in the usual dorsal position. Artificial heat very imperfectly applied did not suffice to prevent the usual morphia fall.

The full details of these cases are noted in the following table:

	Before morphia.	15 minutes later when heat was applied.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.	2½ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 45....	38.3	37.6	37.7	37.7	37.6	37.6	37.6	37.6	37.6	37.4	37.2
No. 46....	37.5	36.5	37.6	37.7	37.8	37.7	37.7	37.7	37.5	37.5	37.5
No. 47....	38.6	38	37	36.8	36.4	36.1	36.1	36.2	36.2	36.3	36.4
Average.	38.5	37.7	37.4	37.4	37.3	37.1	37.1	37.1	37.1	37	37

(X) *The effect of artificial heat upon the temperature curve produced by ether alone* (cf. Curve I, Chart 1).

No. 48. Weight 9 kg. Patient confined on a table in the usual dorsal position with an electrothermal pad under his back, and well protected with blankets. An effort was made to force the temperature up by keeping the animal very warm and deeply anæsthetized. The temperature of the room was 25° C.; that of the electric pad varied from 44° to 52° C.

The body temperature before anæsthesia was 39.2° C.; in one-quarter of an hour 39.7° C.; in half an hour to 40° C.; in three-quarters of an hour 41.1° C.; in one hour 41.2° C.; in one and a half hours 41.3° C.; in one and three-quarters hours 41.5° C., making a total rise of 2.3° C. (4.14° F.) in one and three-quarters hours. At this point death suddenly occurred, possibly from an overdose of ether, though it is probable that the great increase of temperature was the chief factor.

(XI) *The effect of artificial heat upon the temperature curve produced by morphia, ether and operation.*

No. 49. Weight 7.4 kg. An abdominal operation under ether anæsthesia two and a half hours after 16 mg. of morphia had been given hypodermically; artificial heat applied and the patient well protected with blankets. The room temperature 24° C. Body temperature at the beginning of anæsthesia was 37.5° C.; in one-quarter of an hour 38° C.; in half an hour 38.2° C.; in three-quarters of an hour 38.5° C.; in one hour 38.9° C.; in one hour and a quarter 39.2° C.; in two hours 39.8° C.; then continued stationary for half an hour, but in two and three-quarters hours there was a slight fall to 39.2° C.; in three hours to 38.3° C.; in three and a quarter hours to 37.5° C.; in three and a half hours to 37.2° C.; in three and three-quarters hours to 37° C.

No. 50. Weight 6 kg. Abdominal operation under the same conditions as No. 49. Body temperature of the animal at the beginning of ether anæsthesia had fallen to 36.4° C. During the first hour and a quarter there was a slight rise followed by a fall of 0.5° C., owing to cooling of the heating apparatus. On removing the ether and artificial heat a gradual rise of body temperature occurred, amounting to 1.1° C. in one and a quarter hours.

	½ hrs. after morphia, when ether was started.	15 min. after ether was started.	30 minutes.	45 minutes.	1 hour.	1¼ hours.	1½ hours.	1¾ hours.	2 hours.	2¼ hours.	2½ hours.	2¾ hours.	3 hours.	3¼ hours.
	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.	°C.
No. 49..	37.5	38	38.2	38.5	38.9	39.3	39.8	39.8	39.8	39.2	38.3	37.5	37.2	37
No. 50..	36.4	36.2	36.4	36.5	36.4	35.9	36	36.2	36.4	36.7	37	...	...	..
Avg....	36.9	37.1	37.3	37.5	37.6	37.6	37.9	38	38.1	37.9	37.6	37.5	37.2	37

(XII) *The effect on the body temperature of warming the ether vapor before inhalation* (cf. Curve II, Chart 1).

The animals were confined (as in Group II) on the operating table in the usual dorsal position, unprotected, without morphia, and anæsthetized with warmed vapor of ether.

No. 51. Weight 8 kg. Temperature of room 26.6° C. The body temperature before anæsthesia was 38.9° C.; 15 minutes after anæsthesia it was 39° C.; in half an hour 39.2° C.; in three-quarters of an hour 39.3° C.; in one hour 39.4° C.; in two hours 40° C., and in three hours 40.6° C., making a rise of 1.7° C. (3.1° F.). For one hour after ether was removed there occurred a rapid loss of temperature amounting to 3° C. (5.4° F.), where it remained stationary for one hour, and then commenced to slowly rise.

No. 52. Weight 7.5 kg. Temperature of room 21° C. Body temperature before anæsthesia was 38.8° C. Under the anæsthesia the temperature remained stationary for three hours, when the anæsthetic was discontinued. During the next half hour the temperature dropped rapidly, reaching 38° C.; there it remained stationary for half an hour, and the observations were discontinued.

Animals that were being etherized under the usual conditions in the same room and at the same time showed the usual fall of temperature.

CLINICAL OBSERVATIONS.

For comparative purposes an effort was made in the surgical clinic to note the variations in temperature under the usual operating room conditions and to determine if possible whether the customary precautions were sufficient to prevent loss of temperature and whether postanæsthetic complications bore any apparent relation to such a loss. Observations were made upon one hundred and sixty-five patients in whom ether anæsthesia was produced by the open-drop method. The shortest period of anæsthesia in which the temperature was noted was thirty minutes, the longest four and three-quarters hours. Many of the operations were of a major type, such as osteoplastic craniotomy, hysterectomy, amputation of the breast, nephrectomy, cholecystectomy, etc.

The temperature, taken by rectum immediately before starting and immediately after the removal of the anæsthetic showed the average loss to be 0.51° C. (0.92 F.) varying from a rise of .77° C. (1.38° F.) after a four-and-three-quarters-hours anæsthesia for the removal of a cerebellar tumor, during which time the patient was kept dry and warm, to a loss of 1.66° C. (2.99° F.) after a one-and-one-half-hour anæsthesia for a simple appendectomy and unilateral oophorectomy, during which time the patient lay on a cold, rubber-covered table, the abdomen having been flushed with antiseptic fluids and covered with wet towels.

A number of these patients with postoperative subnormal temperatures have been followed to the wards, and even though surrounded by the usual heaters they are apt to complain of being cold when questioned soon after recovering from the anæsthetic. Though I have had no opportunity of following the body temperature of patients subjected to major operations under local anæsthesia, it is quite conceivable that, if they are given, as is customary, a preliminary hypodermic of morphia, and are subsequently kept wet during the operation, that a fall of temperature may occur under these circumstances just as in the laboratory experiments. Thus the postoperative pulmonary complications which are known to follow laparotomies or other operations under cocaine might be explained.

Of the 165 anæsthesias, 25 were for osteoplastic craniotomies, during which the patients were kept dry and well pro-

tected. The average loss of temperature in these instances amounted to 0.18° C. (0.32° F.) against a loss of 0.57° C. (1.02° F.) in the remainder, many of them being abdominal or thoracic operations with the patient more or less exposed and wet during the anæsthetization.

The temperature of the operating room was noted in one hundred and fourteen instances: twenty-one cases, etherized at a room temperature below 24.4° C. (76° F.) had an average loss of 0.75° C. (1.35° F.); thirty-one cases in a room with a temperature of from 24.4° C. to 26.6° C. (76° to 80° F.) had an average loss of 0.69° C. (1.24° F.); forty-nine cases with a room temperature of from 26.6° C. to 29.4° C. (80° to 85° F.) had an average loss of 0.35° C. (0.63° F.); fourteen cases with a room temperature of from 29.4° C. to 32.2° C. (85° to 90° F.) had an average loss of 0.26° C. (0.47° F.); three cases with a room temperature above 32.2° C. (90° F.) had an average loss of 0.07° C. (0.13° F.).

Sixty-five anæsthesias were produced by ether alone; two by the gas-ether sequence; ninety-three by the ethyl chloride-ether sequence, and five by the chloroform-ether sequence. The sixty-five anæsthesias produced by ether alone had an average loss of body temperature of 0.60° C. (1.10° F.); the ninety-three produced by the ethyl chloride-ether sequence had an average loss of 0.55° C. (0.99° F.). Thus the various methods of beginning the narcosis seem to bear only slight relation to the variation in body temperature.

The effect of warming the ether vapor before inhalation is very marked. In twenty-six patients anæsthetized by this method the loss of temperature averaged 0.16° C. (0.29° F.) against a loss of 0.57° C. (1.02° F.) in the one hundred and forty cases anæsthetized under similar operating-room conditions by the open-drop method. On noting the temperature before and after anæsthesia in eleven patients in whom the character of the operations necessitated the exposure of a large surface of the body, six were anæsthetized with warmed vapor, and their average loss of temperature was 0.43° C. (0.77° F.). The five patients anæsthetized under similar operating-room conditions by the open-drop method had an average loss of 1.1° C. (1.98° F.). This shows a difference of .67° C. (1.2° F.) in favor of warmed vapor over the cold anæsthetic.[9]

The results of these studies support the previous observations made by Kappeler, Allen and Mills, and justify the conclusions:

(1) That chloroform produces a loss of body temperature approximately equal to that produced by ether.

(2) That surrounding the field of operation with wet towels will very greatly increase the loss of body temperature and should therefore be studiously avoided.

(3) That the loss of temperature produced by ether narcosis will not be greatly increased by the preliminary administration of a moderate dose of morphia.

(4) That the excessive application of heat to an individual while under the influence of morphia will lessen the usual loss of body temperature from this drug, and that the additional administration of ether under these circumstances may lead to a rise in body temperature rather than the expected fall.

(5) That warming the ether vapor before inhalation will likewise prevent the loss of body temperature, or may actually increase it in a degree proportionate to the temperature of the vapor and also to that of the operating room. An undue

[9] The subject of warm anæsthesia is not a new one, for J. T. Clover, in 1873, devised a double current apparatus (Brit. M. J., March 15, 1873, pp. 282-283) in which the expired air served to warm the ether.

Hawksley (Brit. M. J., August 7, 1873, p. 177) placed the ether chamber in a vessel of water kept at a temperature of 100° F., the ether vapor being conveyed to the patient through a tube.

J. T. Clover (Brit. M. J., July 15, 1876, pp. 74-75) described a new apparatus for administering nitrous oxide gas and ether singly and combined. The ether chamber was constructed so as to fit in a vessel containing hot water, so that the ether would be kept at a temperature of 68° F., or 73° F. if the room were cold. He later improved upon this (Brit. M. J., January 20, 1877) by constructing a portable regulating ether inhaler with a closed hot water compartment.

George Foy (Anæsthetics, Ancient and Modern, p. 141) describes a nitrous oxide apparatus in which the gas is heated by passing through a closed chamber containing hot water, situated between the rubber bag and the face piece.

James T. Gwathmey (Med. Rec., New York, October 14, 1905; N. York State J. M., February, 1908, pp. 68-72; Am. J. Surg., July, 1908, pp. 212-214) has done much to show the advantages of warm anæsthesia over cold. He combined the good features of the Braun and Harcourt inhalers, making a three-bottled apparatus by which four different strengths of ether vapor could be given. The chloroform or ether vapor is forced through hot water which is placed in the third bottle. Dr. Gwathmey discarded this third bottle when he constructed his improved apparatus, and surrounded the remaining bottles (one for chloroform and one for ether) with a closed metal box containing thermolite.

H. Warren Buckler (Maryland M. J., April, 1908) uses an apparatus which consists of a small air pump run by an electric motor, which forces air in an ordinary air-water gasometer filled with very hot water. The stored air is heated and drawn off at will and passes through the ether chamber of a Clover inhaler.

Haun (München. Med. Wchnschr., November 14, 1907, Vol. LIV, No. 47) heated chloroform to 38° C., and then administered it by the drop method, and found it very advantageous. Many others likewise have heated both ether and chloroform by placing the container in a hot water bath and then administering the anæthetic by the drop method.

Many of these methods of warming anæsthetics are either inadequate or too complicated. The method that I have adopted is to convert the liquid anæsthetic into vapor and then heat the vapor to the desired temperature. This can be accomplished by any of the ordinary vaporizers, such as the Gwathmey, Souchon, Junker or Braun type, or by a simple vaporizer constructed out of a six- or eight-ounce bottle, the afferent tube extending well to the bottom of the bottle and the efferent tube only through the cork. In this way air is forced to the bottom of the bottle and bubbles up through the liquid anæsthetic on its way to the warming apparatus. This apparatus consists of an inner chamber with a capacity of about 300 cc., in which are coiled several feet of copper tubing. On the outer side of this chamber, which is filled with hot water, is a second chamber with a capacity of about 300 cc. This is filled with thermolite. This heater will continue warm for four or five hours without being reheated, and can be used for warming ether, chloroform or nitrous oxide gas. When attached to a Gwathmey vaporizer it makes a small, compact apparatus, which can be carried in an ordinary handbag.

elevation of body temperature from this source is doubtless injurious; the object should be to maintain an even temperature.

(6) That in a human patient kept warm and dry during anæsthesia the loss of temperature will be very much less than when the body is wet and exposed, and, furthermore, the fall in temperature is less under ordinary conditions of anæsthesia in a room with a temperature above 26.6° C. (80° F.) than in a room of a lower temperature.

(7) That patients consequently should not only be kept dry and warm, but should be anæsthetized in a room free from draughts and should not be transferred to a cold room even after the anæsthetic is discontinued.

(10) That with such profound variations in body temperature as have been observed, with many of the patients complaining of being cold even after they have been returned to their beds, it perhaps is not surprising that post-anæsthetic pulmonary complications are not uncommon.

POSTOPERATIVE PULMONARY COMPLICATIONS.

By John Homans, M. D., Boston, Mass.

Improvement in the methods of administering anæsthetics has accompanied, but has hardly kept pace with, the progress of surgery in general. Postoperative pulmonary complications continue to be of relatively frequent occurrence. The statistics from different sources, however, show great variability in this respect, and the questions naturally arise: (1) How far is the administration of an anæsthetic by inhalation responsible for these complications? (2) Are there other factors, in addition to the anæsthesia, of etiological importance? (3) Will a perfected technique and greater skill in administration serve to lessen their frequency?

This subject was brought forcibly before me by several cases which have occurred in the practice of Dr. M. H. Richardson, of Boston, to whom I am indebted for permission to study and publish them. They presented symptoms of extensive and sometimes multiple areas of dry pleurisy, and in one case, signs of consolidation of a whole lobe. These conditions were followed by pulmonary embolism or phlebitis, or both, in such a way as to make it clear that the earlier lesions were infarctions and had no actual relation to the anæsthetic. If such instances of obvious embolic infarcts occur, may not others, unrecognized, serve as the origin of pneumonia, abscess or gangrene?

The subject of the origin of postoperative lung complications has been vigorously discussed of late years in Germany. Figures taken from various German clinics show percentages of mortality due to this cause, after abdominal operations, varying from 0.56 per cent to 12.5 per cent. The mortality has been from 25 per cent to 60 per cent of the morbidity. The figures of v. Lichtenberg (1) are as follows:

Reference.	Number of Laparotomies.	Mortality due to Lung Complications. Per cent.
Körte (Bibergeil)	3909	3.5
Czerny	1302	3.9
von Angerer (Gebele)...	1196	6.43
Kümell (Grimm)	1754	2.5
von Mikulicz (Henle)...	1787	8.00
von Mikulicz (Kausch)..	1881	2.4
Krönlein	1409	0.56
Trendelenberg (Läwen).	1829	5.4
Lexer (Wolff)	976	12.5

Trendelenberg's (2) statistics show 1.8 per cent mortality from pneumonia for all operations, which contrasts with 5.4 per cent for laparotomies.

Other figures show that, with the exception of operations on the mouth and throat, these complications are most likely to follow abdominal operations, of which those on the stomach are by far the most prolific source, with operations on the gall-bladder and pelvic organs furnishing a fair proportion.

Operations.	Number of Cases.	Died.	Died of Lung Complications.	Percentage of all Deaths due to Lung Complications.
Stomach	2176	623(28.63%)	181(8.31%)	29.05%
Bile Passages.	1042	132(12.66%)	20(1.92%)	15.15%
Herniæ	1601	60(3.74%)	15(0.93%)	25.00%
Goitre	3526	34(0.96%)	15(0.42%)	44.00%
Gynecological	3280	257(7.83%)	50(1.53%)	19.45%

The mortality due to pulmonary disease following operations on the stomach is highest in cases of cancer, regardless of the nature of the operation. As to the relative frequency of lung complications following inhalation, as against local anæsthesia in these cases, it seems clear that while the morbidity is fully as high under local anæsthesia, the mortality is generally much lower. Concerning the character of the lesion found in the lungs, Bibergeil (3), in an analysis of 283 cases from Körte's clinic, found 98 cases of lobular pneumonia (25% fatal), 27 cases of hypostatic pneumonia, and 10 cases of lobar pneumonia (of which one showed multiple emboli in the pulmonary artery).

These rather meager figures present the variations in different clinics as well as the importance of the subject in general. More would be superfluous, in view of the fact that without analysis of the conditions under which the operations were performed, particularly with regard to the use of trained anæsthetists, and without bacteriological and autopsy findings, they add little to the accurate knowledge of the subject.

Taken as a whole, cases presenting postoperative disease in the lungs may be divided into those in which the exciting cause arrives by the air passages and those in which it arrives by way of the blood- or lymph-vessels. To the first class belong broncho-pneumonias, variously called ether, aspiration

or inhalation pneumonias. These form, or have in the past formed, the larger proportion of all cases. The following is a typical history:

R. C. C., a large, healthy man. *Operation:* Gastroenterostomy for an extensive duodenal ulcer. Morphia and atropine given before operation: anæsthetic started with gas and the ether given with cone: mouth and throat full of mucus during entire operation: breathing difficult.

Evening of same day, some cough, and following day, constant effort to raise sputum. Pulse 120; temperature 99.2° F.; respiration 26.

Second day after operation, marked cyanosis, labored breathing, abundant purulent sputum, coarse râles throughout both lungs, and dullness with bronchial breathing and fine râles in right lower back. Temperature 102° F.; respiration 25-30; pulse rapid and weak.

Third day, same condition, with signs of consolidation in lower left back. Lower temperature.

Fourth day, râles clearing up; temperature falling.

The consolidation cleared up in about a week after operation. The most acute period of the disease lasted about three days, during which time the patient appeared very sick.

This case, regarding it as one of broncho-pneumonia, would seem to be due primarily to the anæsthesia, for with each inspiration mucus had been drawn into the trachea from the mouth and pharynx in spite of efforts to drain the throat and allow free advent of air.

In connection with this aspect of the subject, it is desirable to sum up in more or less detail the results of experimental work done with the object of showing the effect of inhalation narcotics on the air passages and lungs. Work on the quëstion of immunity or the want of it toward bacterial invasion during the administration of anæsthetics should be mentioned.

Offergeld (4) administered ether by several methods to guinea-pigs, rabbits and cats, and killing the animals at various periods after narcosis, studied the pathological changes in the lungs.

Giving ether alone by means of an apparatus which fitted the face in such a way as to allow only the air which entered through the apparatus with the ether to reach the bronchial passages—a "closed method"—and with a period of anæsthesia lasting from seventy to eighty minutes, he obtained the following results. Some of the animals died in several days, and showed at autopsy typical broncho-pneumonia. Others which seemed well, if killed in two or three days showed lungs nearly sound macroscopically but with some areas of induration, which, on section proved to be areas of broncho-pneumonia. In the finer air passages were found desquamation of epithelium, slight hæmorrhages, and fatty degeneration of epithelial cells; in the bronchi some desquamation and a little blood, mucus and pus.

Anæsthetized by an "ether-oxygen" method none of the animals succumbed, and they revived more quickly than after anæsthesia by ether alone. Some suffered from marked bronchitis on the first day, and if sacrificed at this stage showed small isolated patches of consolidation, a thickened and injected bronchial mucosa with some desquamation and extravasation of blood. In some instances the peribronchial tissues were involved.

Using the "open" or "drop" method, Offergeld obtained still more favorable results. There were no deaths from the anæsthetic. The animals were killed one to eight days after narcosis. The early conditions showed an injection of the submucous bronchial vessels with points of hæmorrhage; a slight disarrangement and very slight fatty degeneration of epithelial cells; a little mucus in the lumen of the bronchi; air only in alveoli; no fatty degeneration of alveolar cells. Autopsies after two days showed a normal condition with a disappearance of the fatty degeneration.

This is quite a contrast to conditions found after the "closed" methods where the destruction of epithelium required at least four days for repair in mild cases. The difference consisted in the formation of new cells to replace tissues destroyed in the "closed" anæsthesias as against regeneration of slightly injured tissues in the "open." But in experiments with frequently repeated narcosis by the "drop" method at intervals so short that regeneration had not time to take place, the same extreme degeneration and inflammatory change could be caused as in the "closed" methods.

Other experiments of similar character were performed by von Lichtenberg (5) with chloroform, and especially with chloroform and oxygen. He used guinea-pigs which, according to him, take any anæsthetic badly. He found very constantly atelectasis, emphysema, desquamation and hæmorrhage into bronchioles, often broncho-pneumonia.

Poppert (6) etherized dogs with fitted masks and concentrated ether vapor. Most of the animals were killed by the anæsthetic and showed constantly in the lungs hyperæmia, hæmorrhage and less often œdema. One animal was etherized on two consecutive days. It lay on the left side and inhaled much mucus and possibly vomitus, dying on the second day with typical broncho-pneumonia of the left lung. Poppert also experimented with ether and chloroform mixtures. He considered chloroform less dangerous than ether, and ether more harmful the greater its concentration.

Another line of investigation was pursued by Hölscher (7). He studied the secretion of mucus in the mouth and air passages of dogs and rabbits under both ether and chloroform anæsthesia, especially with relation to the amount and distribution of the inhaled mucus. If some easily traced coloring matter were placed in the mouth, and the animals killed during narcosis, the following facts became apparent: that if the mouth were not properly drained the mucus travelled to all parts of the lung—to the whole right lung if the animal lay on its right and to the left lung if on its left side; that increased violence of respiration due to obstruction in the throat caused increased inhalation of mucus; that with good drainage of the mouth (head hung over to one side) almost no mucus penetrated the bronchi; that the air passages were excited to slight hypersecretion which they themselves were capable of taking care of if not interfered with; that ether did not inhibit the movements of the ciliated epithelium; and

finally, that chloroform excited less secretion than ether. He considered that hypersecretion was due not only to local but also to central influences.

Still another consideration has a bearing on the influence of inhaled anæsthetics in the causation of pulmonary complications. This concerns the local resistance to bacterial invasion which exists in the lungs. Leaving aside the complicated question of how bacteria reach the lungs,[1] there seems to be no doubt of their existence there from time to time in greater or less numbers even in a state of health. Pneumonia has been produced in rabbits by the inhalation of dust particles and exposure to cold (11). Snel (12) experimented with guinea-pigs, which though susceptible to anthrax, do not become infected when virulent cultures are placed in the trachea. Ether or chloroform administered to animals so prepared caused death with dissemination of the anthrax bacillus through the lungs and other organs. Animals anæsthetized for only a short time did not succumb, and this was the case also if the anæsthetic was not given until an hour after the introduction of the organisms.

Observations of this kind are interesting in relation to cases of broncho-pneumonia of the type already mentioned. There is little or no doubt that improved technique in the administration of ether does much to reduce the frequency of these accidents, and precautions suggest themselves.

It would hardly be worth while to mention the many conditions generally accepted as favoring postoperative pneumonia if it were not that many of them have a bearing on still other sources of danger to the lungs. Old age, feeble heart action, arteriosclerosis, alcoholism and cachexia from any cause are contra-indications to operation as much with relation to the heart as to the lungs. A previous slight bronchitis, catarrh or emphysema is an obvious cause for stasis and auto-infection as has been shown by the statistics from Körte's clinic (2).

Among causes arising during operation are excessive cooling brought about by improper covering, by the use of cold fluids or gauzes in the abdomen, or by interference from the anæsthetic with the body's heat production. Loss of blood, wound infection, inhalation of mucus, and over-anæsthetization are other important considerations. Postoperative influences include too long rest in bed, enfeebled circulation, lack of proper lung movements due to a painful abdominal wound, too tight a swathe, or meteorism. These latter conditions have been long dwelt on as causes of pneumonia. It is said that many patients with epigastric wounds cannot raise the excess of mucus caused by anæsthetization and so accumulate septic material in the lungs. Hypostatic pneumonia, which ought perhaps to be classed with inhalation pneumonia, may be brought about as often in this way as by enfeebled circulation, pressure of the liver against the right lobe of lung, or any other of the causes to which insufficient aeration is attributed.

Experimental observations such as I have described, considered in relation to these unfavorable conditions, might well account for many of the postoperative pulmonary complications. The striking contrast between the statistics of Krönlein and those of other German surgeons quoted in the beginning of this paper, is in strong support of this view. Krönlein (17a) during the period covered by his report, made use of an expert anæsthetist, who gave ether by the "open" method. He allowed practically no preparation of the patient on the table, doing away with the cooling from fluids and wet coverings. He shortened the period of anæsthesia by beginning the operation at the earliest moment permitted, seeing to it that the operator was ready before the anæsthesia was begun. I have no note of other precautionary measures or of the class of operations performed, but with only this information I should be willing to credit to Krönlein's system the pulmonary mortality of only 0.56 per cent—strikingly low as compared with the mortality in other clinics.

However much protection is afforded by efforts of this sort, there still remain operations of certain kinds which, even when performed under cocaine, are not infrequently followed by pulmonary disease. In these cases injury to the lungs by the anæsthetic is often out of the question. Are they to be regarded as due to the various favoring influences mentioned above, or are there more definite sources of injury to the lungs not connected with inhalation anæsthesia? Gastrectomies, gastroenterostomies, gastrostomies, abdominal injuries involving tears or contusions of bowel, and to a lesser degree, hernia-strangulations, are in a considerable percentage of cases followed by pneumonia.

Gottstein's figures (13) for cocaine operations from Mikulicz's clinic are as follows: Operations 212; abdominal 138; all other 74; of the 74 only one case (operation for hypertrophied prostate with purulent cystitis) led to pulmonary symptoms; of the 138, in 13 per cent postoperative bronchitis or pneumonia occurred. This percentage excludes all cases in which vomiting might have influenced the conditions and also those in which the symptoms appeared more than three days after operation. Henle's (14) figures from the same clinic show that while the pulmonary morbidity in stomach surgery (the principal cocaine operation) is as high with local as with general anæsthesia, the mortality with the former is distinctly lower.

As a cause for lung involvement after such operations, infection through the lymphatic system has been suggested. A number of cases are mentioned by Goebel (15) in support of this "lymphatic" hypothesis. In two of them a general anæsthetic was used, but the sudden onset of pulmonary symptoms is inconsistent with the ordinary type of "ether-pneumonia." Two others were performed under local cocaine injection.

Case I.—Healthy man; kicked in abdomen; four hours later resection of torn bowel under ether: in four hours more elevation of temperature and respiration; next day many areas of consolidation; death in eight days. Autopsy showed a diffuse process resembling croupous pneumonia. Wound and region of resection clean. No obvious embolism.

[1] Articles on the permeability of intestines to bacteria, and their transference to lungs (8), (9), (10).

Case II.—Gastroenterostomy for cancer. Ether. Practically the same results followed.

Case III, (16).—Man, aged 72: œsophageal stenosis; moderate emphysema and peripheral arteriosclerosis; cocaine; gastrostomy; pneumonia beginning on same day with dullness in lower right back. Death in one and one-half days. Autopsy showed croupous pneumonia of right middle lobe; no embolism; wound clean.

Case IV, (16).—Man, aged 56: œsophageal cancer; no cachexia; gastrostomy; cocaine; pneumonia on same day with consolidations scattered through both lungs; sputum on second day contained colon bacillus; recovery.

Other instances of pneumonia are cited in which the fluid in the sac of a strangulated hernia was found to contain the same organism as that isolated from the lungs.

Taking the above cases into consideration and having in mind the investigations on the permeability of the intestinal walls to bacteria and other foreign substances (8, 9 and 10), Goebel undertook to demonstrate an anatomically direct pathway from bowel wall to lung. He showed that insoluble coloring matters injected into the walls of the small intestine found their way through the lymph-vessels of the mesentery, the lymph-glands at its base, the thoracic duct and so to the lung. This process took place in a few hours. The same experiments were then carried out with tetragenus broth and cultures of *Bacillus prodigiosus,* and though the lungs were found infected in from one to twenty-four hours, the course of the organism could not be traced.

Kelling (17), in a paper read before the German Surgical Congress in 1905, points out other possible routes between the mesenteric or peritoneal lypmh stream and the lungs, particularly through the diaphragm and retroperitoneal systemic veins.

Though this lymph-stream hypothesis may explain what appear to be embolic processes, whose origin is presumably in regions where the portal circulation carries blood not directly to the heart but to the liver, embolism from the veins of the stomach may reach the lungs by anastomoses with œsophageal veins, and the veins of the lower intestine may communicate through rectal veins. Inflammatory processes about the appendix may start a thrombosis in retroperitoneal veins having a direct route to the lungs. Abdominal operations in such regions together with those on the uterus and adnexa may furnish a source of embolism (25) (26) and gross pulmonary embolism is too well known to require comment. But that lesser degrees may serve as a source of pneumonia is illustrated by the following cases which have occurred in the practice of Dr. M. H. Richardson:

Case I.—Anæmic woman; hysterectomy for fibroids; ether; uneventful convalescence until eighth day when "dry pleurisy" appeared in right side, accompanied by temperature of 101° F., rapid pulse and respiration. Symptoms disappeared after two days. A week later while patient was still in bed a thrombosis occurred in left thigh. Recovery. This appears to have been a case in which pleurisy was due to an infarct. The subsequent thrombosis in the leg was probably the sequence of the same process which caused the pleurisy.

Case II.—Uterine fibroids, cyst of broad ligament, complicating advanced abdominal pregnancy. Ether. Extensive pelvic operation with drainage. No sepsis subsequent to operation. Pneumonia on eighth day; elevation of temperature falling in several days with access of fever on twelfth day. As the patient was starting for home, sudden death occurred, with symptoms of pulmonary embolism. No autopsy. In this case the connection of the pneumonia with embolism is not proven, but the subsequent fatal embolism makes this seem a probable course.

Case III.—Woman with bad ischio-rectal abscess; thorough operation under ether; gauze packing; favorable convalescence, the temperature falling to normal in four days; on fifth day "dry pleurisy" in left back with signs of consolidation of lower left lobe; temperature of 102° F., becoming irregular later on, but always elevated; rectal wound clean and granulating well; same condition for six days when she suddenly died, supposedly of pulmonary embolism. No autopsy. Here again the conditions in the lung seemed to be independent of the anæsthetic—apparently a pneumonia or extensive infarct. Subsequent death from pulmonary embolism suggests embolic origin.

Case IV.—Middle-aged man. Acute perforative appendicitis with local abscess of several days duration; operation under ether; wound drained. Anæsthetic well taken and condition after operation favorable.

Second day after operation characteristic pain of dry pleurisy in right chest. Pain constant. Steadily rising pulse until fourth day when pulmonary embolism occurred; collapse; pulse high; temperature low; respiration 30-35. Patient remained in critical condition with frequent periods of partial collapse and difficult breathing until eleventh day when symptoms of "dry pleurisy" again appeared in the same side, the temperature running up to 102° F. Twentieth day phlebitis discovered in both legs. Twenty-third day death from pulmonary embolism. Autopsy by Dr. F. B. Mallory showed thrombi in both pulmonary arteries, the older, occluding all branches on the left and adherent to the walls, and the more recent occluding the right. In the right common iliac and femoral veins were found the thrombi from which embolism had occurred. A small retroperitoneal vein in the appendicular region was also thrombosed. No direct relation between the appendicular wound and iliac thrombosis was found. There was no evidence of infection. The right lung showed six or eight sharply defined infarctions with a fresh exudate on the pleural surface. The bronchi were empty. There was no œdema or exudate elsewhere. The report states that "the slight exudate in the lung and the organizing pneumonia were secondary to the infarction and probably some slight bronchial infection."

This case illustrates the course of a thrombosis giving rise to many small emboli, causing multiple infarctions and finally death from embolism. The original thrombus was not infected though it was found near an appendix abscess.

That thrombosis may be caused in intestinal vessels by handling, strangulation, or tying off veins, and that embolism will sometimes occur from this source has been shown often in animal experimentation (18) and (19); and Payr (20) has demonstrated that in some animals embolism from various parts of the portal circulation may reach the stomach and thence the lung. In fact, whatever the route, pulmonary embolism has been experimentally brought about in animals from sources within the portal circulation. I find no record, however, of an experimental pneumonia having been set up in this way.

In human beings embolic pneumonias undoubtedly occur, usually arising from thrombosis in systemic but possibly also in portal veins. There is simply a matter of degree and a

little infection thrown in between a harmless infarct, an embolic pneumonia, and a fatal pulmonary embolism. Certainly avenues of infection are furnished in cases in which an uninfected embolus reaches the lung. The air passages may play a part in introducing the organisms, or these may preexist in the field. On the other hand, that all infarctions, or even a majority of them, set up a pneumonia is far from the truth.

Recent statistics from v. Eiselsberg's clinic (26), collected with special reference to postoperative embolic processes, cover 6871 cases. Among these there were pulmonary complications in 263 (3.8 per cent). Of the 263 cases, 57 were of embolic origin. This number represents 0.83 per cent of all patients operated on and 21.6 per cent of those with postoperative disease in the lungs. Among these 57 cases were 23 of fatal pulmonary embolism, 20 of infarcts, and 14 of purulent embolic processes.

It is difficult to classify the diverse forms of postoperative pulmonary complications, but they may be grouped as follows:

I. Cases depending on narcosis, variously known as inhalation, aspiration or ether pneumonias; characterized by a general broncho-pneumonic process, purulent sputum, early appearance and short duration.

II. Cases of stasis in the lungs known as hypostatic pneumonias. These cases probably merge into the first and third classes but their characteristic is that they are caused by enfeebled circulation and inability to keep the lungs clear.

III. Cases depending on embolism, either from lymph-vessels or veins. If from the former, admitting the existence of such a process, the onset is sudden, and occurs soon after the operation. The disease resembles the lobar type. If from veins the pneumonia resembles the lobar type again but varies greatly. It appears when the circulation becomes active enough after operation to dislodge emboli from a thrombus. This class of case merges into the fatal embolism which generally occurs from the second to the fourth week and may include abscess or gangrene according to the severity, extent and character of infection of the process.

Against these accidents of surgery certain remedies readily suggest themselves. If heed is paid to a careful preparation of the patient, especially with regard to the good condition of the mouth, air passages and bowels; if operations of choice are only performed when the patient's circulatory system is at its highest point of efficiency; if operations of emergency, when the patient is not at his best, are conducted as rapidly and with as little waste of the vital energy as is consistent with efficiency, a local anæsthetic being used whenever it is of practical advantage, and if the most "open" method of inhalation anæsthesia, together with the smallest possible amount of the anæsthetic, is employed, the dangers from the first and second classes of lung complications will have been reduced to a minimum. Trained anæsthetists above all are to be desired. Certainly the quoted results from Krönlein's clinic (17a) obtained along these lines are far in advance of those published from other sources abroad.

As to the embolic class of cases, while there is much to be gained from these same precautions, yet it seems as if the technique of the operator with regard to injuries to tissues, the condition of the patient as regards sepsis and the individual predisposition to thrombosis must be cardinal influences. The present tendency to shorten rest in bed, with care and nursing calculated to keep the lungs and circulatory system in a high state of efficiency is an excellent one as avoiding danger of this sort. In this way massage and passive motion, as prophylactic measures, are useful weapons against thrombosis.

Careful study of such cases, especially the exact nature of the morbid process and the bacteriology, both in the living and in the dead will do much to clear up the subject. Many failures now regarded as unforeseen accidents may be prevented. "Unavoidable calamities" of surgery is a term which, however comforting to the surgeon, should be constantly limited in its application, and from under this head many cases of postoperative disease of the lungs should be eliminated.

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NOTES ON NEW BOOKS.

Ticks, a Monograph of the Ixodoidea. By GEORGE H. F. NUTTALL, M. D., etc., and CECIL WARBURTON, W. F. COOPER and L. E. ROBINSON. Part I, Argasidæ. Price 5/. (*Cambridge, England: University Press, 1908.*)

This first part of a work which is intended to deal with the classification, structure and biology of Ticks in extenso, with a full consideration of the previous work of others, promises to be a very interesting contribution to a field of medical zoology which is growing in importance daily. In this section, in addition to the thorough description of the various species of Argas, Ornithodoros, etc., with the life history as far as known, of each, much of which is based on original experiments and observations by the authors, there is in the biological section a very careful study of the relations of *A. persicus* and *A. reflexus* to spirochætosis in fowls, and the transmission of the spirochæta of African relapsing fever (*S. duttonii*) by *Ornithodoros moubata*. The rôle played by these ticks in the transmission of filaria and of bacterial infections is also discussed.

The make-up of the book is excellent as to type, paper and plates, and the extra index to the bibliography, arranged for transfer to card catalogues is a valuable innovation.

The remaining sections are to appear within a year and will be looked for with interest by all who are working in the related fields of medicine and zoology. T. R. B.

Diseases of the Skin and the Eruptive Fevers. By JAY FRANK SCHAMBERG, A. B., M. D., etc. (*Philadelphia: W. B. Saunders Company, 1908.*) Price, $3.

It is quite a pleasure to welcome this latest addition to the list of dermatological text-books. It is admirably adapted to the needs of medical students. The descriptions of the eruptions are so clear and concise that the appearance of a disease can readily be imagined. The facts about etiology and pathology are stated without verbiage. The arrangement of diagnosis of many of the diseases is excellent, the points considered being placed opposite one another in parallel rows under the names of diseases considered, so that differentiation can be more easily made. It is not, however, as complete as it might be. Treatment is given in a satisfactory manner, though methods and dosage are to some extent neglected. Occasionally faults are found; for instance, a bath of washing soda is recommended for the relief of urticaria. A special chapter describes the methods of actinotherapy and radiotherapy.

An abundance of excellent illustrations is the most attractive feature of the book. Experience has taught the publishers the value of illustrations in text-books on dermatology, and so they have been very liberal with their expenditures in this work. The photographs are well selected and show detail admirably.

Considerable space is given to the exanthemata, and the skin manifestations are exhaustively considered. In addition, mention is made of the various eruptions occurring in the course of typhoid and typhus fevers, cerebro-spinal meningitis, influenza, malaria, rheumatic fever, dengue, miliary fever, angina and tonsillitis.

However, the author should remember that all medical students are not so erudite as he is. For this reason such terms as *causa causans, contagium vivum, origo mali*, etc., are to be avoided. It takes too long to look for a translation, and so they are usually passed over or are misinterpreted.

The Baby. A Book for Mothers and Nurses. By DANIEL ROLLINS BROWN, A. B., M. D. (*Boston: Whitcomb & Barrows, 1908.*) Price, $1.00.

There is a surplusage of books on the care of babies, and this small one takes its place in the rank and file. It has no distinctive qualities to make it stand forth prominently. It is clearly and simply written, and can safely be put in the hands of those to whom it is dedicated.

Arteriosclerosis: Etiology, Pathology, Diagnosis, Prognosis, Prophylaxis, and Treatment. By LOUIS M. WARFIELD, M. D., etc., with an introduction by W. S. THAYER, M.D. (*St. Louis: C. V. Mosby Medical Book Co., 1908.*)

Dr. Thayer, in his introduction, emphasizes the laxity with which the term arteriosclerosis is made to cover many obscurities in diagnosis, and points out the great gaps in our knowledge as to its nature and causes. The book itself is a brief review of the subject of arterial disease treated rather from the standpoint of the practitioner than that of the pathologist. Although not profound, it will surely be found useful, especially in those chapters which deal with prophylaxis and practical suggestions as to treatment.

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